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Radiological Evaluation of Skin Nodules in Cancer Patients

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Abstract

Background: Skin and subcutaneous nodules are frequently met findings whether presenting as primary skin malignancies, benign lesions, or secondary metastatic deposits. The radiological evaluation of these nodules plays a pivotal role in diagnosis, staging, treatment planning, and monitoring therapeutic responses. Early differentiation of benign versus malignant lesions can prevent unnecessary invasive procedures and guide appropriate treatment strategies. Moreover, recognizing metastatic skin nodules may signify systemic disease progression, necessitating comprehensive oncologic evaluation and intervention.

Aim of Study: Evaluate the radiological features of skin and subcutaneous nodules, including primary skin malignancies, skin metastases and benign skin lesions in patients with known primary malignancy together with measuring CT and MRI specificity and sensitivity in differentiating benign and malignant skin lesions.

Patients and Methods: This study was a retrospective study conducted in National Cancer Institute. A total of 151 patients with skin lesions were evaluated. Patients were either new cases coming with newly discovered skin lesion or patients with known primary malignancy coming with either a newly recognized skin lesion or for routine metastatic work up which unveiled a clinically unrecognized skin lesion. Patients underwent CT or MRI based on clinical scenario. Radiological findings were correlated with either pathology or 6 month follow-up in cases not indicated for biopsy.

Results: Out of a total of 151 patients, 57 patients (37.7%) had benign skin lesions and the other 94 (62.3%) were malignant skin lesions, with 51 cases with primary skin malignancy and 43 cases with distant skin metastases. CT sensitivity was 93.02%, specifically 82.76%, while MRI sensitivity reached 94.44% with 84.21% specificity.

Conclusion: With a high sensitivity and specificity for malignancy, this study concludes that CT and MRI are useful radiographic tools for evaluating skin and subcutaneous nodules. Integration of imaging, histological, and clinical data is still crucial. Future developments in artificial intelligence and imaging technology could substantially increase the accuracy of diagnoses in this area.

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Key Words: *Subcutaneous nodules – Cutaneous lesions – Computed Tomography (CT) – Magnetic Resonance Imaging (MRI) – Contrast-enhanced imaging.*

Introduction

SKIN and subcutaneous nodules are frequently met findings whether presenting as primary skin malignancies, benign lesions, or secondary metastatic deposits. The radiological evaluation of these nodules plays a pivotal role in diagnosis, staging, treatment planning, and monitoring therapeutic responses. Despite their significance, the imaging characteristics of these nodules often overlap, posing challenges in distinguishing between benign and malignant entities **[1].**

Primary skin malignancies, such as melanoma, basal cell carcinoma, and squamous cell carcinoma, exhibit diverse radiological features depending on their size, depth, and level of tissue invasion. On the other hand, benign skin lesions, including lipomas, epidermoid cysts, and dermatofibromas, typically demonstrate well-defined, non-infiltrative characteristics. Metastatic involvement of the skin and subcutaneous tissues is commonly seen in advanced cancers, with lesions manifesting as ill-defined, infiltrative masses, often associated with enlarged and pathologically enhanced lymph nodes **[2].**

Imaging modalities, particularly computed tomography (CT) and magnetic resonance imaging (MRI), are essential tools in assessing these nodules. CT scans offer excellent spatial resolution, enabling the detection of calcifications, fat content, and enhancement patterns, while MRI provides superior soft tissue contrast, crucial for evaluating lesion composition and infiltration. Features such as cystic components, enhancement patterns, fat suppression signals, and diffusion characteristics help delineate benign from malignant lesions. Advanced techniques, including diffusion-weighted imaging

(DWI) and contrast-enhanced sequences, have further improved diagnostic accuracy **[3].**

Studies have highlighted that benign lesions, such as lipomas or simple cystic formations, generally exhibit non-enhancing or homogeneously enhancing patterns on imaging. In contrast, malignant lesions often present as heterogeneously enhancing masses with infiltrative margins, central necrosis, and restricted diffusion. Additionally, radiological signs of metastatic disease include speculated margins, dirty fat planes, and associated lymphadenopathy with cystic degeneration or enhancement **[4].**

The clinical implications of accurate radiological assessment are profound. Early differentiation of benign versus malignant lesions can prevent unnecessary invasive procedures and guide appropriate treatment strategies. Moreover, recognizing metastatic skin nodules may signify systemic disease progression, necessitating comprehensive oncologic evaluation and intervention **[5,6].**

In addition to CT and MRI, Positron emission tomography-computed tomography (PET-CT) has emerged as a powerful imaging modality in the evaluation of skin and subcutaneous nodules, particularly in cancer patients. By combining metabolic and anatomical imaging, PET-CT provides unique insights into the biological activity and precise localization of lesions, making it an invaluable tool in oncologic imaging **[7,8].**

This study aims to evaluate the radiological features of skin and subcutaneous nodules, including primary skin malignancies, skin metastases and benign skin lesions in patients with known primary malignancy together with measuring CT and MRI specificity and sensitivity. By analyzing imaging characteristics and correlating them with histopathological findings, this research seeks to enhance diagnostic precision and provide a framework for effective radiological assessment in oncologic care.

Patients and Methods

Our study was a retrospective study conducted in the National Cancer Institute. A total of 151 patients with skin lesions were evaluated in the period from 1/1/2024 to 1/1/2025.

Inclusion criteria:

- New patients with a skin lesion need radiological evaluation as a primary step to determine need for biopsy.
- Patients with known primary malignancy with newly discovered skin lesion distant from the site of primary that requires radiological evaluation.
- Patients with known primary malignancy having routine metastatic work up CT which unveiled a clinically unrecognized skin lesion.

Exclusion criteria:

- Contraindication to contrast material.
- Claustrophobia in patients requiring MRI.
- Locally advanced malignancies that infiltrated the skin, or skin lesions across the surgical tract of the primary tumor (these lesions were considered part of local disease).

Patient preparation:

Before the examination all patients had renal function tests performed together with full clinical history and explanation of the procedure that will be performed.

Examination techniques:

- Patients included in the study underwent post contrast CT or pre and post contrast MRI based on clinical scenario. Radiological findings were correlated with either pathology or 6 month follow-up in cases not indicated for biopsy.
- CT was performed in the scenario of routine metastatic follow up which unveiled a skin lesion while MRI was performed for dedicated assessment of a skin lesion arising either as a primary clinical symptom in a new case or as a new symptom in a known cancer patient.

CT Technique:

Conventional CT study was performed on a Toshiba Aquillon 16 device. Patients were positioned in supine anatomical position headfirst with the abdomen centered parallel to the gantry. Scout images first were acquired. Ultravist 300 contrast was injected 70-100ml (0.1mL/kg) with 30-40mL saline chaser at 3-5mL/s. subsequently contrast enhanced images were obtained in portal venous phase: 60-80 seconds after contrast injection.

Cases having metastatic work up had CT chest, abdomen and pelvis. CT neck or maxillofacial was added to patients with lymphoma or primary head and neck malignancy.

MRI technique:

- MR imaging was performed using the Achieva, Phillips Medical Systems, Best, Netherlands, Release 2.6, Level 3 high field system (1.5 Tesla) closed magnet unit.

- Precontrast T1 and T2 WI, Fat Suppression images were obtained.
- Diffusion-weighted sequence with multiple b-values (b-0, 50, 400 & 800). ADC maps were calculated from the diffusion-weighted images utilizing specific software at the workstation.
- Gadolinium-based MRI contrast agent is administered intravenously in approximately 0.2mL/kg (0.1mmol/kg) at a rate of 10mL per 15 seconds. Then post contrast T1-weighted sequences were performed in the axial, coronal and sagittal planes.

CT and MRI Image analysis:

CT and MRI studies were examined by a specialized radiologist with 15 years of practice. The primary signs of benignity of the lesion in both CT and MRI were being completely cystic, or fatty with no post contrast enhancement. Supplementary signs included stability in size and radiological features for more than six months to one year together with absent pathological lymph nodes.

Benign MRI features:

- Fat signal (being high on both T1 and T2 weighted images and dark on fat saturation sequences.
- Totally calcified lesions (being dark on all sequences) show homogeneous faint contrast or non-contrast uptake in post contrast studies and facilitated diffusion on DWIs.

Malignant MRI features:

- Ill-defined solid lesions with avid or non-homogeneous enhancement, central break down and restricted diffusion and associated malignant enhancing lymph nodes.
- Complex cystic lesions with enhancing solid nodules.

PET CT technique:

Patients fasting for 6 hours are injected with 185-370 MBq of 18F FDG, depending on body weight . 50 to 60 minutes after IV injection of 18F FDG, the patients were examined in the supine position with arms elevated, and CT scanning was started at the level of skull base with the following parameters: 40mAs; 130 kV; slice thickness, 2.5mm; pitch, 1.5. PET over the same region was performed immediately after acquisition of the low dose CT images. Image interpretation was accomplished by experienced two nuclear medicine physicians.

Pathological correlation:

- CT and MRI results correlated with pathology. Biopsy and pathological correlation were performed for all patients with suspected malignant features. Accordingly, CT and MRI false negative and positive results were determined and calculated.
- Patients with benign findings were put under regular follow-up (three months on average) with a minimum of six months to detect any change in features or new indication for biopsy.

Statistical analysis:

Data was coded and entered using the statistical package for the Social Sciences (SPSS) version 28 (IBM Corp., Armonk, NY, USA). Data was summarized using mean, minimum and maximum in quantitative data and using frequency (count) for categorical data.

Results

Our study included 151 patients with skin and subcutaneous nodules and masses, with 88 males and 63 females. Mean age at presentation is 45.04 years (range 0-90 years). With 40 patients in the pediatric age group (<18ys) and 111 adult patients (>18yrs).

Among the 151 cases, the head and neck were the commonest location of the lesions in about 70 patients followed by 40 in the thoracic region, 18 in the abdomen, 20 in the extremities and 3 cases all over the body.

Pathological diagnosis: Out of total 151 patients, 57 patients (37.7%) had benign skin lesions and the other 94 (62.3%) were malignant skin lesions, with 51 cases with primary skin malignancy and 43 cases with distant skin metastases Table (1).

Table (1): Pathological cell type.

Cell types	Number
BCC, SCC (non-melanoma skin cancer)	17
MM	8
Breast cancer	11
Lymphoma	10
Fibromatosis, NF, lipomas	12 cases each
Bronchogenic ca, desmoid tumor and fibrous hystocytoma	5 cases each
Hemangioma	4 cases each
Thyroid cancer, RCC and NB	3 cases each
Soft tissue sarcomas (OS, RMS, fibro sarcoma, synovial sarcoma, etc...)	24
MPM, RMS, AML, uterine cancer, trichilemmal and inclusion epidermoid cyst	2 cases each
Cancer colon, synovial sarcoma nevus, mycosis fungoid, xeroderma pigmentosa cutaneous melanosis ...etc.)	1 case each

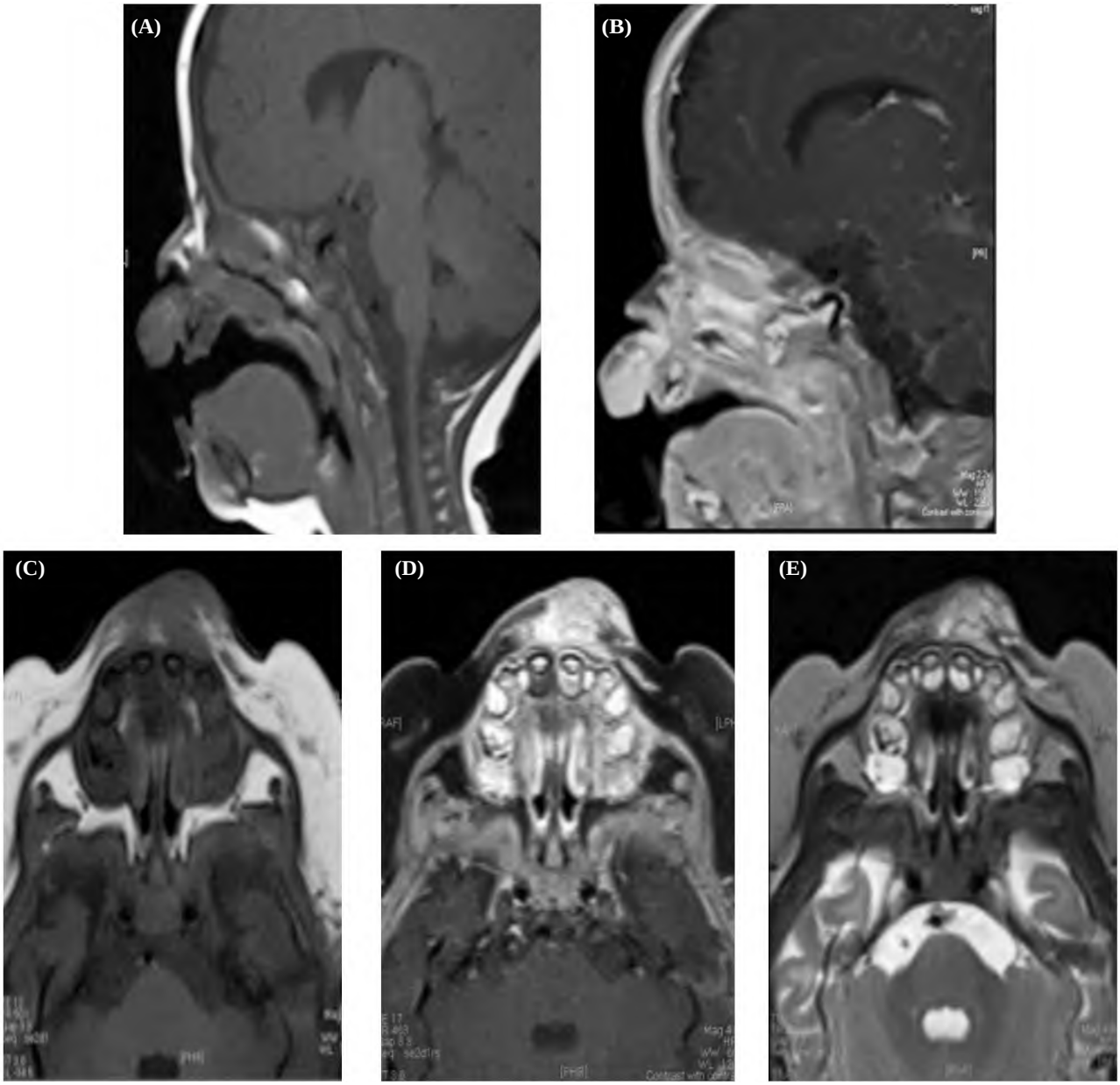

Fig. (1): Sagittal T1pre (A) and post contrast images (B), Axial TI pre (C) and post contrast, (D) and T2 (E), of maxillofacial of 5 years old boy with upper lip high T2 avidly enhancing lesion (hemangioma).

In benign skin lesions fibromatosis, neurofibromas and lipomas were the most encountered pathologies, and in the second order came desmoid and fibrous histiocytoma. Less encountered lesions were hemangioma (Fig. 1) and inclusion epidermoid cyst.

Regarding distant skin metastases breast cancer was the post common primary malignancy (Table 2) Fig. (2).

Regarding primary malignant skin lesions, non-melanotic skin malignancy was encountered more than melanotic malignancy. Fig. (3).

Table (2): Primary tumors with distant metastases.

Total	43	100%
Breast cancer	11	25.85%
Lymphoma	8	18.6%
RCC	3	6.97%
MPM	2	4.65%
RMS	2	4.65%
Thyroid cancer	3	6.97%
Synovial sarcoma	1	2.32%
Colon cancer	1	2.32%
Uterine cancer	2	4.65%
Bronchogenic carcinoma	5	11.62%
NB	3	6.97%
Aml	2	4.65%

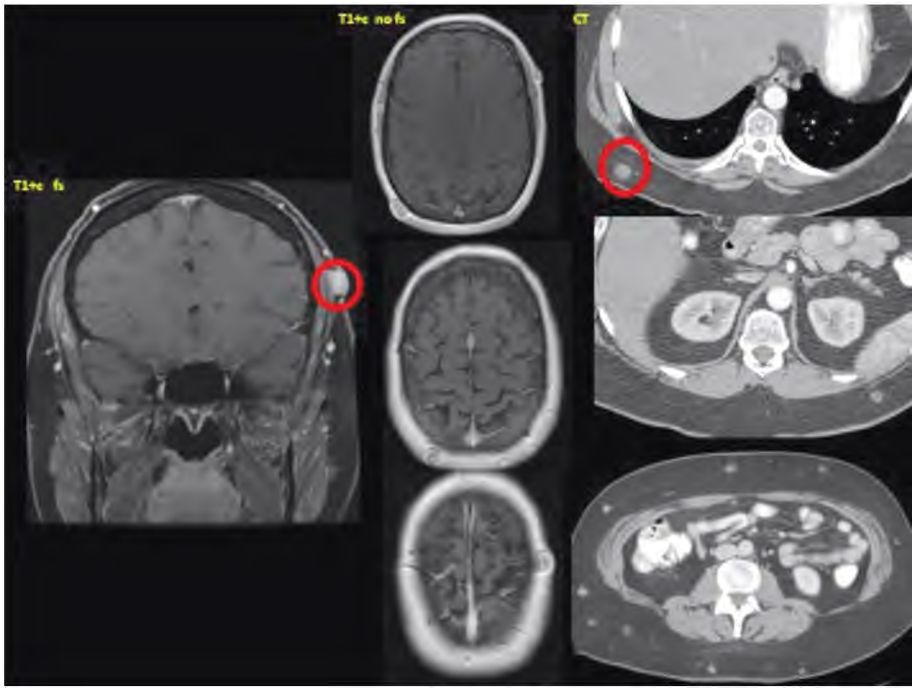

Fig. (2): A known case of breast cancer presenting with multiple skin lesions: Post contrast MRI and CT images revealed multiple enhancing skin nodules (enhancement was perceived in mri). Pathology proved metastatic breast cancer.

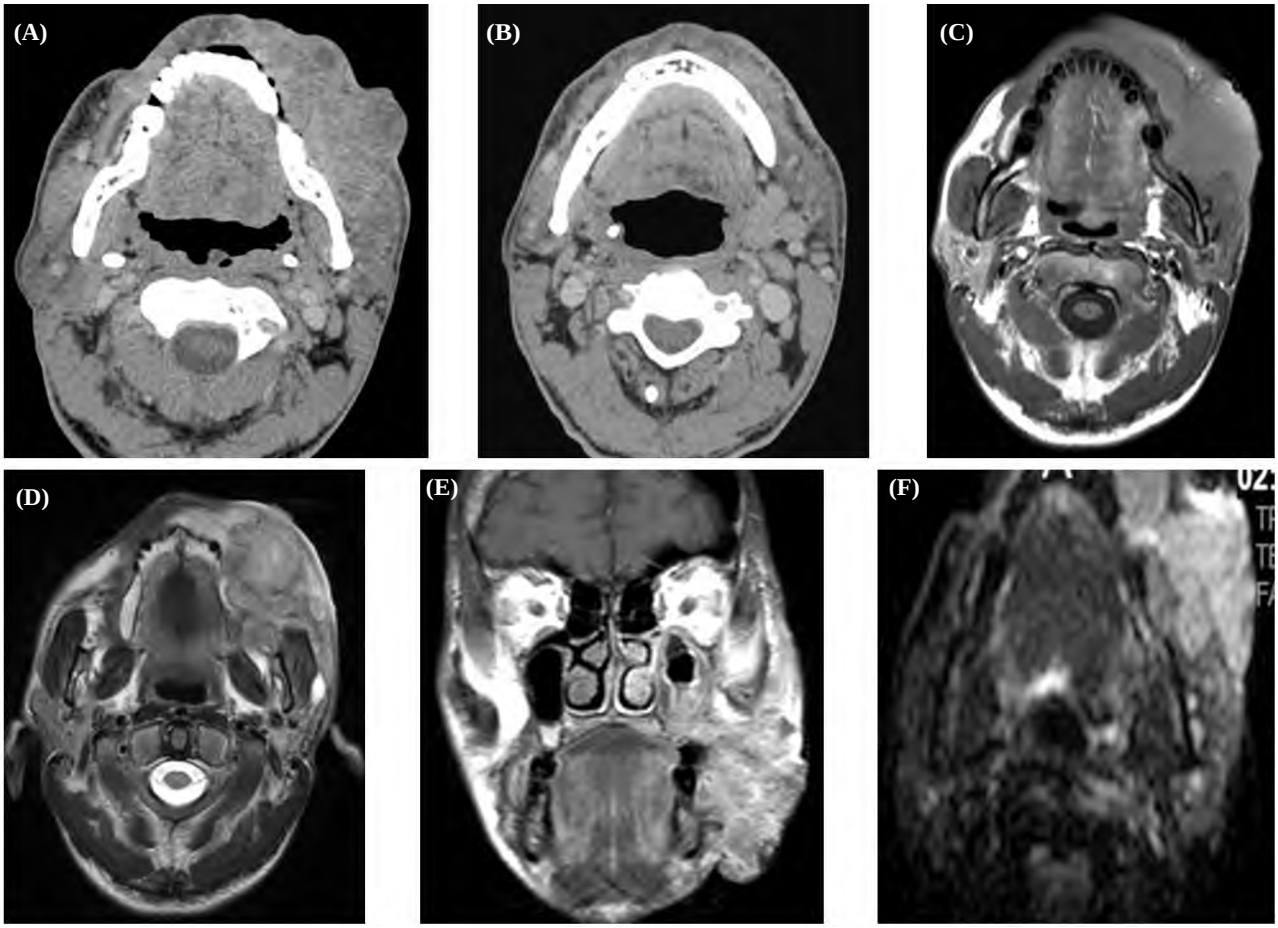

Fig. (3): A and B axial CT scan of the maxillofacial for 58 old male show, left buccal soft tissue ill-defined ulcerating mass lesion with central breakdown, it shows inhomogeneous contrast uptake and destruction of the underlying maxillary bone with bilateral enlarged lymph node. MRI (T1 (C)) & T2 (D) & post contrast T1 (E) images and ADC (F)) showing low T1, high T2 and inhomogeneous contrast uptake, with bone marrow affection, it shows restricted diffusion, Pathology: SCC (squamous cell carcinoma).

CT Results Table (3):

Table (3): CT findings in relation to pathology.

Positive	85 malignant	Negative	30 benign
True positive	80	True negative	24
False positive	5	False negative	6

- False negative cases were six as follows.
- Two cases with AML suggest inflammatory process, pathology revealed myeloid sarcoma figure 4 & three cases with well-defined benign looking small lesions, pathology revealed soft tissue sarcomas. One case with primary uterine cancer with CT show small benign looking solitary skin lesion, pathology revealed metastatic lesion.

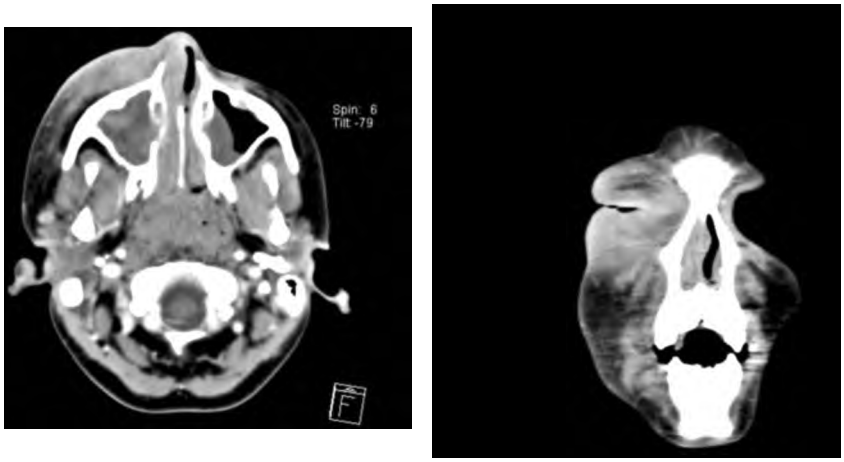

Fig. (4): Axial and coronal post contrast CT images of the sinuses for AML patient with maxillary sinusitis with pre maxillary and periorbital soft tissue thickening thought to be part of inflammatory process but pathology revealed myeloid sarcoma.

- False positive cases.
- 5 lesions, however, were histopathological proven to be benign skin lesions. (3 cases of fibromatosis, 1 case with nevus mucoepidermoid and 1 case epidermal inclusion cyst.

According to the previous numbers both sensitivity and specificity were calculated with the CT sensitivity = 93.02% and specificity = .82.76%.

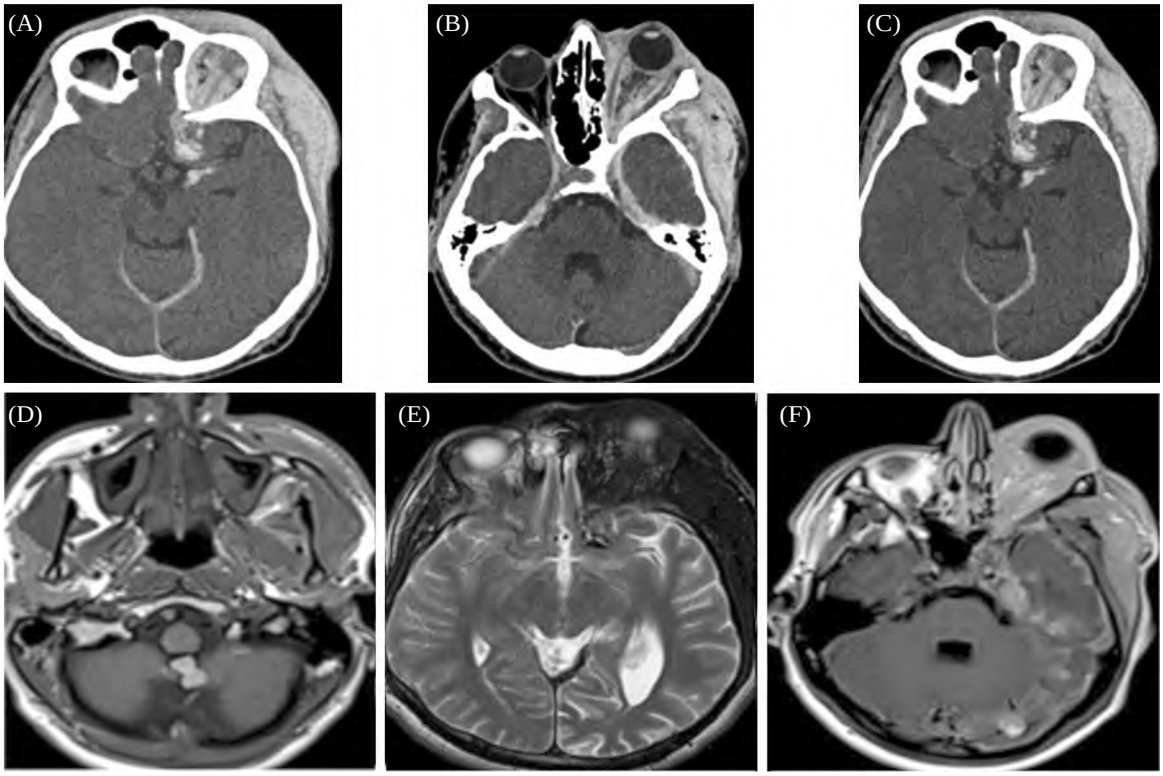

Fig. (5): Post contrast axial CT brain A-C, and MRI (T1 (D) & T2 (E)) and post contrast T1 (F)) for the 21-year old male with left proptosis, dark bluish swelling of the upper third of the left hemi-face, images show Diffuse mass lesion involving the left upper face with low T2 signal extending along V1,V2 nerve tract associated with meningeal lesions pathology revealed neurocutenous melanosis.

MRI results Table (4):

Table (4): MRI findings in relation to pathology.

Positive	37 malignant	Negative	18 benign
True positive	34	True negative	16
False positive	3	False negative	2

According to the previous numbers both sensitivity and specificity were calculated with the MRI sensitivity = 94.44% and specificity = 84.21%.

Findings:

- Among the 50 cases that performed MRI the false negative cases were two that were pathologically proven to be malignant (2 cases of well differentiated liposarcoma).
- False positive cases were three cases (fibrous histiocytoma, fibromatosis and neurocutenious melanosis Fig. (5).
- The cases which matched pathological diagnosis displayed malignant criteria in the form of ill-defined solid lesions with avid or non-homogeneous enhancement, central break down and restricted diffusion and associated malignant enhancing lymph nodes.
- Complex cystic lesions with enhancing solid nodules.

Regarding the PET/CT:

Only four cases in our study had PET CT. Two cases were described as benign, having no or low grade FDG uptake merging with radiological features of benign CT criteria and the other two lesions described as malignant lesions and were pathologically correlated Fig. (6).

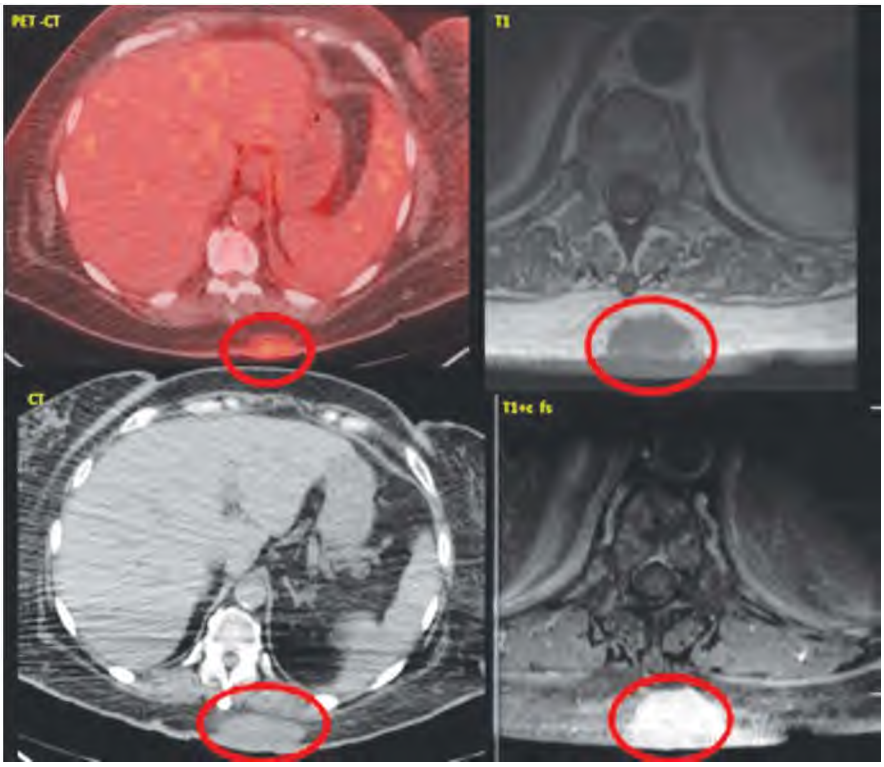

Fig. (6): PET CT, axial CT, Pre and post contrast MRI images for 61-year-old female with known uterine cancer, PET / CT revealed midline mid back well-defined subcutaneous lesion with FDG avid lesion, SUV max 10, MRI show avidly enhancement Pathology revealed metastatic lesion.

Discussion

This study's findings emphasize the essential function of radiological imaging in differentiating benign from malignant skin and subcutaneous nodules, consistent with prior literature that identifies the diagnostic difficulties arising from overlapping imaging characteristics **[2]**. Our results demonstrate that CT and MRI are highly effective tools for this purpose, with sensitivities of 93.02% and 94.44%, and specificities of 82.76% and 84.21%, respectively.

These figures are consistent with prior studies, such as Thawait et al. **[3],** who reported similar diagnostic accuracies for advanced imaging modalities in skin cancer evaluation.

Our analysis revealed a notable predominance of malignant lesions (62.3%) over benign lesions (37.7%), with breast cancer identified as the most prevalent original malignancy linked to distant skin metastases. This finding corroborates global cancer statistics, which identify breast cancer as a leading cause of metastatic disease [6].

However, a contributing factor for this result is that patients who have suspicious malignant features are those who are directed by their clinicians for seeking radiological help.

Our diagnostic criteria were further validated when we found that the radiological characteristics of malignant lesions, such as restricted diffusion, heterogeneous enhancement, and ill-defined margins, were like those reported by Lamer and Bui-Mansfield [5].

Notable instances of false-positive and false-negative results were also found in the study. Lesions that first appeared benign but were later shown to be malignant, such as soft tissue sarcomas and myeloid sarcomas, were among the six false-negative instances on CT. In second look evaluation of myeloid sarcoma in leukemic patients (false negative case in our study) absence of perilesional fat smudging and edema should not be overlooked when differentiating between malignancy and infections.

These misclassifications emphasize the limitations of relying solely on imaging for definitive diagnosis, particularly for lesions with atypical presentations. Similarly, the false-positive cases (e.g., fibromatosis and epidermal inclusion cysts) highlight the need for integrating clinical and histopathological data to improve diagnostic accuracy, as advocated by MacKie [4].

Characterizing complex lesions, like those with cystic components or fat suppression signals, was made easier by MRI's higher soft tissue contrast resolution. The two false-negative MRI instances, which were well-differentiated liposarcomas, highlight the difficulties in identifying low-grade cancers that can pass for benign fatty tumors.

The clinical implications of our findings are significant. Accurate radiological differentiation between benign and malignant lesions can guide appropriate management, reduce unnecessary invasive procedures and optimize treatment strategies [7]. For example, early identification of metastatic skin nodules can prompt comprehensive oncologic evaluation, as seen in our cases of breast cancer metastases.

Skin and subcutaneous nodules provide a variety of diagnostic difficulties, including radiological, histological, and clinical aspects. Our research emphasizes how important imaging is to this diagnostic trio, especially when it comes to distinguishing benign from malignant lesions. In our study 33.8% of cases were primary skin malignancies which go hand in hand with the epidemiological trends showing an increase in the prevalence of skin cancers, particularly those that spread to other parts of the body [6]. This pattern emphasizes how crucial early and precise radiological evaluation.

In our investigation, magnetic resonance imaging (MRI) and computed tomography (CT) emerged as key modalities, each with unique benefits. For preliminary assessments, especially in metastatic workups, CT's great spatial resolution was invaluable in identifying calcifications and fat content. But compared to MRI (84.21%), its poorer specificity (82.76%) indicates inherent limits, like the challenge of describing lesions with modest soft tissue changes. For instance, the six false-negative CT cases which included soft tissue and myeloid sarcomas were misunderstood because of their seemingly innocuous appearance. This is consistent with Thawait et al. [3] who pointed out that early malignant changes may be missed by CT's inherent limitations.

MRI provides optimal superior soft tissue contrast; this was emphasized particularly in complex cases in our study like neurocutaneous melanosis and juvenile hyaline fibromatosis. Regarding melanosis dark signal in T2 and high signal in T1 weighted images, diffuse skin affection with no aggressive features as heterogenous enhancement, infiltration of underlying bone suggests the diagnosis. Equally significant is the presence of the lesions since birth. A pitfall that should be emphasized is that spread along nerves does not exclude benign nature.

Regarding hyaline fibromatosis, bright T2 signal, facilitated diffusion, no underlying bone infiltration together with clinical history of high rate of recurrence. This correlates with Lamer & Bui-Mansfield, [5] who stated that hallmarks of malignancy can be outlined by advanced sequences like diffusion-weighted imaging (DWI) and contrast-enhanced studies, which reveal restricted diffusion and heterogeneous enhancement.

Our well-differentiated liposarcoma false-negative MRI cases highlight a crucial risk: low-grade cancers with a high fat content can be mistaken for benign lipomas. This is in line with Strobel et al. [8] who stressed the importance of using MR spectroscopy and other supplementary techniques in situations that are unclear.

Limitations and future directions:

This study has limitations even if it offers insightful information. PET CT results were limited by the small sample size, future studies to clarify its function in evaluating skin nodules are recommended. Furthermore, new research in radiology suggests that using machine learning algorithms to evaluate imaging aspects could improve diagnostic accuracy even further **[2].**

Recent developments in imaging technology, including contrast-enhanced ultrasound (CEUS) and ultrasound elastography, are promising for increasing the diagnostic accuracy of skin and subcutaneous nodules. Elastography, which measures tissue stiffness, has proven especially helpful in distinguishing benign fibromas from malignant lesions because malignant tumors tend to be stiffer because of their dense cellularity **[9]**, while CEUS offers real-time evaluation of microvascularization, which helps identify aggressive lesions with abnormal blood flow patterns **[10].** These techniques should be further studied in the future.

Conclusion:

With a high sensitivity and specificity for malignancy, this study concludes that CT and MRI are useful radiographic tools for evaluating skin and subcutaneous nodules. For a correct diagnosis, however, the integration of imaging, histological, and clinical data is still crucial. Future developments in artificial intelligence and imaging technology could substantially increase the accuracy of diagnoses in this area.

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التقييم الإشعاعى لعقيدات الجلد لدى مرضى السرطان

أجريت هذه الدراسة الاستعادية لتقييم السمات الإشعاعية لعقيدات الجلد والأنسجة تحت الجلد فى ١٥١ مريضًا بالسرطان بالمعهد القومى للأورام، جامعة القاهرة، باستخدام جهاز التصوير المقطعى وجهاز الرنين المغناطيسى.

وتم قياس دقة التصوير فى التمييز بين الآفات الحميدة والخبيثة، بما فى ذلك سرطانات الجلد الأولية (مثل الميلانوما، وسرطان الخلايا القاعدية/الحرشفية) والنقائل الجلدية (مثل أورام الثدى، الليمفوما).

سجل الرنين المغناطيسى نسب دقة حساسيه أعلى من النسب المسجلة لجهاز التصوير المقطعى.

أظهر التصوير المقطعي حساسية ٩٣,٠٢٪ ودقة ٨٢,٧٦٪.

بينما الرنين المغناطيسى أظهرحساسيه ٩٤,٤٤٪ و دقه ٪ ٨٤,٢١

يعد التصوير المقطعى والرنين المغناطيسى أدوات قيّمة فى تشخيص عقيدات الجلد، حيث يتمتعان بحساسية ودقة عالية فى الكشف عن الأورام الخبيثة. يظل التكامل بين التصوير والفحص السريرى والنسيجى أمرًا حيويًا. يجب أن تركز الأبحاث المستقبلية على تقنيات جديدة لتحسين الدقة التشخيصية تشمل الذكاء الاصطناعى.