Added Value of ^{68}Gallium-PSMA PET/CT over Contrast Enhanced CT in Prostate Cancer Patients

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Abstract

Background: ^{68}Gallium (^{68}Ga) -ligand- (PSMA) is a new radiotracer with great diagnostic potential in prostate cancer patients. The imaging is usually performed using PET/CT system, and PET/MRI system when available. The results of PSMA PET/CT in identifying intra-prostatic disease are very impressive. The use of PSMA PET/CT has a higher detection rate of predicted local or distant metastasis compared to CT. **Aim of the Work:** The aim of this study is to appraise the added value of ^{68}Gallium PSMA PET/CT over the contrast enhanced CT in patients with prostatic cancer. **Patients and Methods:** The study included 29 male patients in this comparative study (their ages ranged from 50 and 75 years, with mean age of 64.28 years), (the mean of PSA level was 16.86 with range from 0.02 to 150 ng/ml) were referred to the PET/CT unit with different scenarios related to prostate cancer (Biochemical recurrence, initial staging and follow up) at MISR Radiology Center "MRC" in Cairo, Egypt using hybrid PET/CT machine (PET/CT 128 slices machine). Comparative ^{68}Ga-PSMA PET/CT and contrast enhanced CT scans were conducted for all patients. Each patient included in the study was subjected to full history taking and reviewing serum PSA and serum creatinine levels. **Results:** ^{68}Ga PSMA PET showed high accuracy in the detection of the prostate cancer, seminal vesicles invasion, local and distant lymph nodes metastasis, lung metastasis, liver metastasis and bone metastasis compared to CECT. **CONCLUSION:** ^{68}Ga PSMA PET showed high ability in the detection of the prostate cancer, seminal vesicles invasion, local and distant lymph nodes metastasis, lung metastasis, liver metastasis and bone metastasis compared to CECT. It was able to exclude or confirm malignancy in cases with CECT suspicious findings of malignancy. The sensitivity and specificity were 82 % and 65 % respectively. However, a larger number of patients and longer-term study are still needed to validate the results of this study.

Key Words: Prostate cancer, Contrast enhanced CT, 68Ga-PSMA PET, PSA.

List of Abbreviations:

CECT: Contrast Enhanced Computed Tomography.
CT: Computed Tomography.
i.v.: Intra venous.
KV: kilo volt.
MA: Milli ampere.
MRI: Magnetic Resonance Imaging.
PCa: Prostate Cancer.
PET: Positron Emission Tomography.
PSA: Prostate Specific Antigen.
PSMA: Prostate Specific Membrane Antigen.
TF: Time of Flight.
68Ga: Gallium-68

Introduction

The 2nd most frequent cancer diagnosis in men and the 5th leading cause of death globally is the prostate cancer (PCa). Prostate cancer (PCa) may be asymptomatic at the early stage and it often has an indolent course that may require only active surveillance. [1]

The positron emission tomography is defined as a tomographic imaging technique that computes the three-dimensional distribution of radioactivity based on the annihilation of photons that are emitted by the positron emitter labeled radiotracers. A non-invasive assessment of the biochemical and the functional processes quantitatively is offered by PET. [2]

68Gallium (68Ga) -ligand- (PSMA) is a new radiotracer with great diagnostic potential in prostate cancer patients. Although there is physiological expression of the (PSMA) in multiple organs, it is overexpressed 100 folds to one 1000 folds in 95% of prostate cancer (PCa) cells. The imaging is usually performed using PET/CT system, and PET/MRI system when available. [3]

Aim of work

The aim of this study is to appraise the added value of 68Gallium PSMA PET/CT over the contrast enhanced CT in patients with prostatic cancer.

Patients and methods

The study included 29 male patients in this comparative study (their ages ranged from 50 and 75 years, with mean age of 64.28 years), (the mean of PSA level was 16.86 with range from 0.02 to 150 ng/ml) were referred to the PET/CT unit with different scenarios related to prostate cancer (Biochemical recurrence, initial staging and follow up) in MISR Radiology Center "MRC" in Cairo, Egypt using hybrid PET/CT machine (Philips ingenuity TF PET/CT 128 slices). Comparative 68Ga-PSMA PET/CT and contrast enhanced CT scans were conducted for all patients. Each

patient included in the study was subjected to full history taking and reviewing PSA and serum creatinine levels. (between March 2020 and December 2020). These procedures are approved by local Ethics Committee. All patients provided a written informed consent.

Inclusion criteria:

- Patients recently diagnosed with prostate cancer.

- Patients with biochemical recurrence.

- Patients under prostate cancer treatment coming for follow up.

- Patients fit for PET/CT examination and contrast injection.

Exclusion criteria:

- Patients with normal PSA.

- Patients not fit for PET/CT examination and contrast injection.

- Patient refused to participate in our study.

Each patient included in the study was subjected to:

- Full history taking.

- Reviewing serum PSA and serum creatinine levels.

- All patients are subjected to ^{68}Ga-PSMA PET/CT scan followed by contrast enhanced CT).

Technique:

- All patients were briefly instructed about our study and duration of examination.

- Proper preparation (regarding proper clothing and metal disposal) instructions were delivered and checked by the aiding nurse.

- Technique was performed using a PET/CT 128 slices machine.

- Patient is asked to empty the bladder immediately before the scan.

- Patient position: Supine, with head fixation and arms rose up.

- PET is performed after the attenuation correction CT study without moving the patient.

- Approximately 9 to 11 bed positions were planned in the three-dimensional acquisition mode for scanning the entire patient in one and half minutes for image acquisition for each bed position. For each of these sets of PET and CT images "fusion" images, combining the two types of data is processed by special software to produce functional and anatomical image simultaneously. Scanning parameters for low dose attenuation correction CT were: 100 MA, 120 KV, pitch of 0.8, collimator

width of (64 X .625), gantry rotation time of 0.5 second and field of view of 50 cm.

- For CECT scanning started cranially at the level of the skull and extended caudally to the level of mid thighs. The total length of CT coverage equals to an integral number of bed positions scan during acquisition of PET data. Injection of 1.5 mL of contrast agent per kilogram bodyweight, with maximum 120 mL and imaged in the portal venous phase 80 seconds after I.V. injection of the contrast agent.

- After examination patient is instructed to drink plenty of water to get rid of any remaining radioactive material and avoid close contact with pregnant women and children for 8 hours after ⁶⁸Ga-PSMA injection.

RESULTS

This study included29 male patients (their aged ranged from 50 and 75 years, with mean age of 64.28 years), (the mean of serum PSA level was 16.86 with range from 0.02 to 150 ng/ml) Table 1.

⁶⁸Ga PSMA PET showed high ability in the detection of the prostate cancer, seminal vesicles invasion Table 2, Figure 1, local and distant lymph nodes metastasis Table 3,

lung metastasis, liver metastasis and bone metastasis compared to CECT. It was able to exclude or confirm malignancy in cases with CECT suspicious findings of malignancy. The sensitivity and specificity were 82 % and 65 % respectively. However, a larger number of patients and longer-term study are still needed to validate the results of this study.

CASES

Case (1)

- **Clinical profile:** A 64 -year- old male patient presented with elevated PSA level (13.3 ng/ml) on routine checkup, patient then pathologically proven with prostatic adenocarcinoma.

- **On contrast enhanced CT (CECT):**

The prostate is mildly enlarged measuring 47x48x46 mm, showing homogenous texture with estimated prostate volume of 54 cc, with no definite prostatic lesion detected. No suspicious lymph nodes, bone lesions, liver lesions or pulmonary nodules. No seminal vesicles invasion.

- **On fused ⁶⁸Gallium- PSMA PET/CT and 3D PET:**
  - A ⁶⁸Ga-PSMA avid lesion is seen at the prostate left peripheral apical/mid zones, achieving 5.8 SUV max.

- o No PSMA avid lymph nodes, bone lesions, liver lesions or pulmonary nodules.
- o No seminal vesicles invasion.

- **Comment:**
  - o The enlarged prostate gland did not show any lesions on the contrast enhanced CT (CECT) but showed a peripherally located lesion of ^{68}Ga-PSMA uptake achieving 5.8 SUV (Fig. 2).

Case (2)

- **Clinical profile:** A 61 -year- old male patient, diagnosed with metastatic prostate adenocarcinoma by treated radiotherapy 2 years ago, presented with recently elevated PSA level (5.5 ng/ml) [i.e. biochemical recurrence].

- **On contrast enhanced CT (CECT):**
  - o The prostate is average in size, measuring 38 x 29 x 31, with estimated volume 18 cc, showing homogenous texture.
  - o No suspicious lymph nodes, bone lesions, liver lesions or pulmonary nodules.
  - o No seminal vesicles invasion.

- **On fused ^{68}Gallium- PSMA PET/CT and 3D PET:**

- o No prostatic PSMA avid lesions detected.
- o A left external iliac PSMA avid regional pelvic lymph node, achieving 6.81 SUV max.
- o Left 9th rib PSMA avid lesion achieving 10.4 SUV max.
- o No PSMA avid liver lesions or pulmonary nodules.
- o No seminal vesicles invasion.

- **Comment:**
  - o The PET confirmed the absence of local prostatic recurrence.
  - o A left external iliac metastatic regional lymph node, showing PSMA avid uptake that was not detected on CECT (Fig. 3).
  - o A left 9th rib metastatic PSMA avid lesion was detected by PET, yet not detected by conventional CECT (Fig. 4).

Case (3)

- **Clinical profile:** A 66 -year- old patient with metastatic prostate cancer, pathologically proven prostatic adenocarcinoma, Gleason score = 9 (5 + 4), the patient is under anti-androgen therapy started 6 months ago and coming for evaluation of the therapeutic response. PSA level=9.6 ng/ml.

- **On contrast enhanced CT (CECT):**

  o The prostate appears average in size measuring 34 X 36 X 27 mm with estimated volume of 17 cc, showing homogenous texture.

  o Multiple lymph nodes enlargement detected in the neck, chest abdomen and Pelvis.

  o No suspicious bone lesions, liver lesions or pulmonary nodules.

  o No seminal vesicles invasion.

- **On fused ⁶⁸Gallium- PSMA PET/CT and 3D PET:**

  o The prostate gland shows high⁶⁸Ga PSMA uptake achieving 29.7 SUV max and both seminal vesicles also show⁶⁸Ga PSMA uptake achieving 12.9 SUV max at the right seminal vesicle.

  o Multiple ⁶⁸Ga PSMA avid lymph nodes detected in the neck, chest, abdomen and pelvis, the one with the highest ⁶⁸Ga PSMA uptake is a para-aortic lymph node achieving 31.8 SUV max.

  o No PSMA avid bone lesions, liver lesions or pulmonary nodules.

- **Comment**:

  o On the CECT the prostate and the seminal vesicles appeared normal, while on ⁶⁸Ga-PSMA PET both showed avid PSMA uptake confirming prostate cancer (Fig. 5) invading both seminal vesicles (Fig. 6).

  o The multiple enlarged lymph nodes detected in CECT, showed high PSMA uptake on ⁶⁸Ga-PSMA PET, confirming its metastatic nature.

Table (1): Shows that mean of age was 64.28 ± 7.7 with range from 50 to 75 years, mean of PSA level was 16.86 with range from 0.02 to 150.

	Mini	**Max**	**Mean**	**Standard Deviation**
Age (yrs)	50	75	64.28	7.70
PSA level (ng/ml)	0.02	150	16.86	27.24

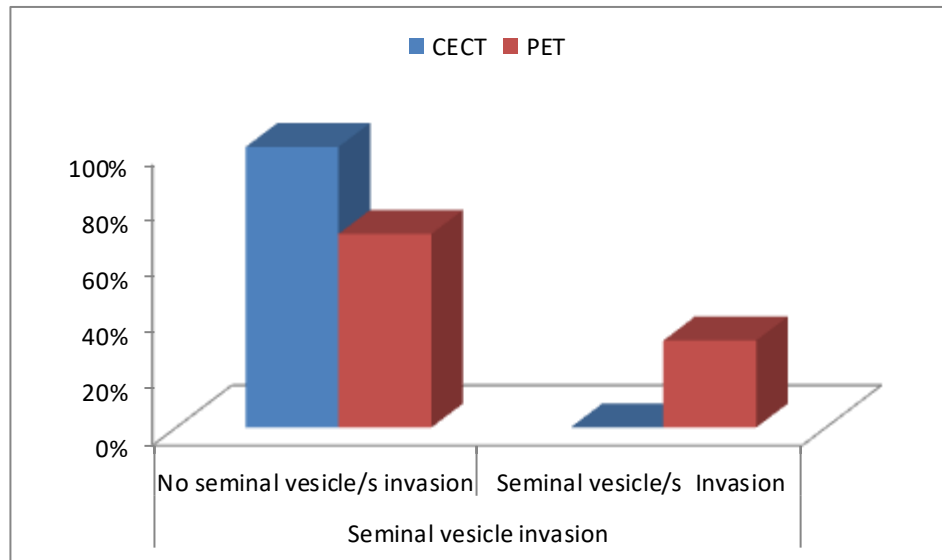**Table (2):** Illustrates the significant increase in Seminal vesicle/s invasion detection in ^{68}Ga PSMA PET CT in comparison to CECT.

		CECT (No.=29)		PET (No.=29)		Chi square test	
		No	%	No	%	x^2	p value
Seminal vesicle invasion	No seminal vesicle/s invasion	29	100.0%	20	69.0%	10.653	0.001
	Seminal vesicle/s Invasion	0	0.0%	9	31.0%		

Table (3): Detection of local and distant lymph nodes metastasis in ^{68}Ga PSMA and CECT.

		CECT (No.=29)		[68]Ga PSMA (No.=29)		Chi square test	
		No	%	No	%	x^2	p value
Local L.N. metastasis	No local L.N. metastasis	19	65.5%	8	27.6%	8.385	0.004
	Local L.N. metastasis	10	34.5%	21	72.4%		
Distant L.N. metastasis	No distant L.N. metastasis	21	72.4%	12	41.4%	5.695	0.017
	Distant L.N. metastasis	8	27.6%	17	58.6%		

Figure (1): Illustrates the significant increase in Seminal vesicle/s invasion detection in ^{68}Ga PSMA PET CT in comparison to CECT.
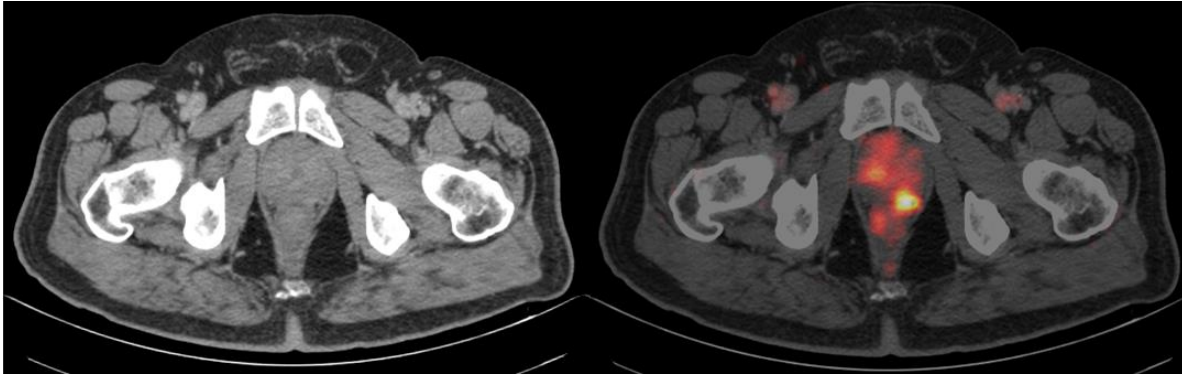
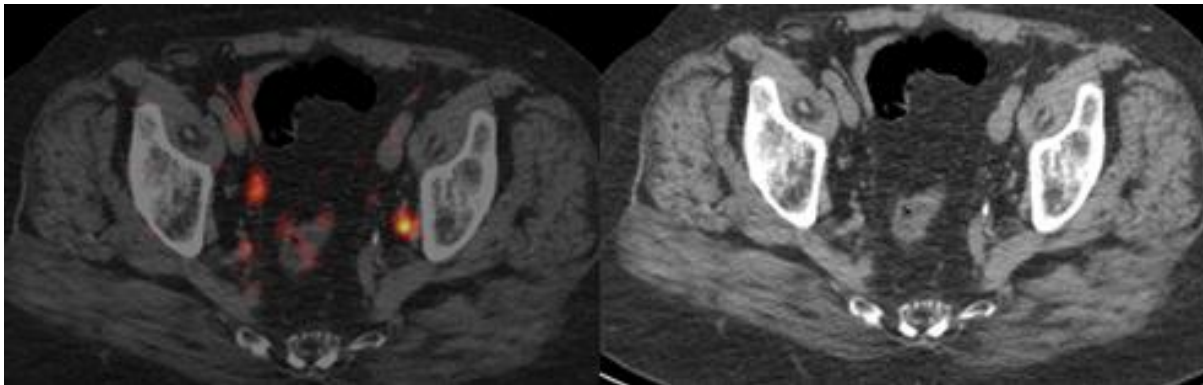**Figure (2):** Axial fused PET/CT and CT images of the pelvis, case 1

Figure (3): Axial fused PET/CT and axial CT images of the pelvis, case 2
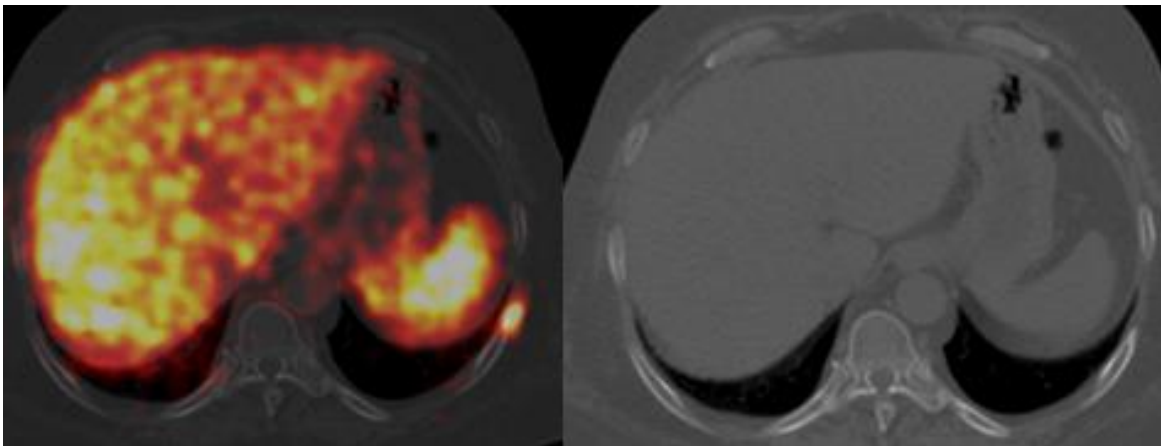

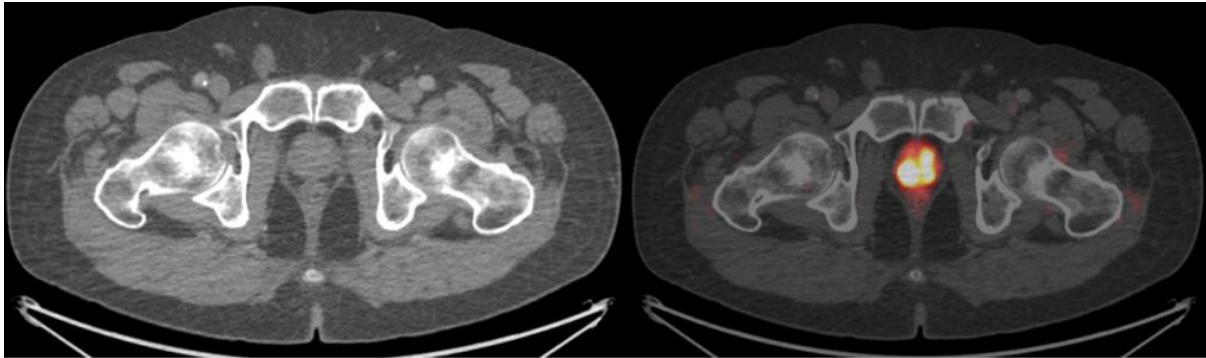**Figure (4):** Axial fused PET/CT and axial CT images of the ribs, case 2

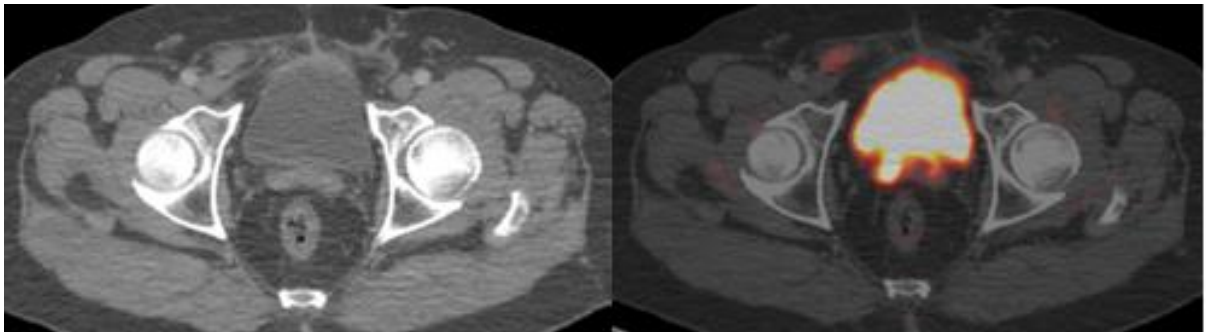**Figure (5):** Axial fused PET/CT and axial CT images of the pelvis, case 3

Figure (6): Axial fused PET/CT and axial CT images of the pelvis, case 3

Discussion

The 2nd most frequent cancer diagnosis in men and the 5th leading cause of death globally is the prostate cancer (PCa). Prostate cancer (PCa) may be asymptomatic at the early stage and it often has an indolent course that may require only active surveillance. [2]

Most prostate cancers use non-glucose metabolic pathways such as fatty acid metabolism or fructose metabolism. So FDG, which is the most widely used PET tracer in oncologic imaging, is of limited use in prostate cancer. [4]

68Gallium (^{68}Ga) -ligand- (PSMA) is a new radiotracer with great diagnostic potential in prostate cancer patients. [3]

Staging of primary lesions by PSMA PET/CT is important in guiding treatment decisions. In patients with positive nodes, a more extensive lymph node (LN) dissection may be performed. In the case of radiotherapy, the fields may be extended to encompass the additional pathology found by PSMA. If widespread metastases are disclosed by PSMA PET/CT systemic therapy may be favored. [5]

68Ga-PSMA PET/CT proved high diagnostic sensitivity in finding of the site of recurrence in patients coming with biochemical recurrence even with low PSA values. This explains the recommendation of European urology association to use 68Ga-PSMA PET/CT in biochemically recurrent patients leading to earlier detection of site of recurrence and accordingly initiate the proper management plan. [6]

The use of PSMA PET/CT has a higher detection rate of predicted local or distant metastasis compared to CT and BS in the staging of patients with biochemical recurrences after radical prostatectomy. [7]

PSMA PET/CT could play a role in sparing biopsies in selected cases when biopsy is relatively contraindicated (e.g. bleeding disorders, absence of rectum). One potential use for PSMA PET/CT is to limit the number of biopsies to the high uptake lesions. [5]

In our study lesions that were visually considered as suggestive of a primary tumor, relapses or metastases of prostate cancer were counted and analyzed with respect to their SUV max. A cut-off value of SUV max 4.0 over the prostate gland was considered as abnormal.

Thus, SUV max values of more than 4.0 and above over prostatic bed (primary or recurrence) were considered as suspicious of malignancy or recurrent tumor. [8]

This cut-off value of SUV max 4.0 was compatible with Hassan et al. (2020) method which considered prostatic tracer uptake as positive for residual/recurrent neoplastic lesions if its tracer uptake was higher than the background activity. [4]

On CT a soft tissue lesion of 1 cm or larger in the prostatic bed or demonstrating contrast enhancement was considered suspicious for local recurrence and reported as such. A lymph node with 1 cm in short axis dimension or those that were smaller, but demonstrated contrast enhancement with irregular margins, were also considered pathological. Lytic and sclerotic bony lesions with ill-defined margins were classified as bony metastases. [7]

The most updated guideline released by the European Association of Urology (EAU) suggests the use of PSMA-PET/CT imaging in any case of biochemical recurrence, i.e., PSA > 0.2 ng/mL, after radical prostatectomy. This recommendation reaches a strong level of evidence, namely when PSMA-PET/CT scan allows the optimization of the treatment strategy. [9]

Conclusion

^{68}Ga PSMA PET showed high ability in the detection of the prostate cancer, seminal vesicles invasion, local and distant lymph nodes metastasis, lung metastasis, liver metastasis and bone metastasis compared to CECT. It was able to exclude or confirm malignancy in cases with CECT suspicious findings of malignancy. Showed sensitivity and specificity of 82 % and 65 % respectively However, a larger number of patients and longer-term study are still needed to validate the results of this study.

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