Utility of Fluorine18 Fluoro-2-deoxy-D-glucose Positron Emission Tomography/Computed Tomography in Metabolic Characterization of Solid Renal Mass Lesion and Localization of Extra Renal Lesions in the Body – A Prospective Study from the Tertiary Care Center in South India

Abstract

Purpose of the Study: Renal mass lesions in majority of the cases are due to malignant etiology and about one-third of them are reported with metastatic lesions at the time of presentation. Thus proper investigational workup is needed for staging and thereby treatment planning. The current fluorine18 fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography (F18-FDG PET/ CT) study was designed to characterize renal mass lesions metabolically and identifying other metabolically active lesions in the body suggesting metastatic disease. Materials and Methods: A total of 24 patients (males -18 and females -6) with a mean age of 53.8 ± 12.3 years were recruited in this study for dual time-point PET/CT scan. All patients with renal mass lesions underwent contrast-enhanced CT prior to PET/CT. Metabolic parameters such as maximum standardized uptake value (max.SUV) with a cut off ≥ 2.5 and retention index (RI) of $\geq 10\%$ were used to label the lesion as malignant and remaining less than cutoff as benign. The final diagnosis of lesion on imaging was confirmed with a histopathological examination (HPE). Results: Using max.SUV cut off value, 17/24 renal mass lesions were characterized as malignant and remaining 7/24 renal lesions of benign etiology. PET/CT showed sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 80%, 75%, 94.1%, 42.8%, and 79.1%, respectively, by considering HPE as a gold standard. Nine patients were diagnosed with distant site involvement suggestive of metastases. Conclusion: F18-FDG PET/CT can efficiently characterize solid renal mass lesion as benign and malignant using metabolic parameters such as max.SUV and RI. In addition, whole-body survey identified distant site involvement in 25% of the patients, thus contributing change in management.

Keywords: Fluorine18 fluoro-2-deoxy-D-glucose positron emission tomography/computer tomography, maximum standardized uptake value, retention index, solid renal mass lesion

Introduction

Solid renal mass lesions are incidentally detected in many patients undergoing diagnostic workup for symptoms unrelated to renal pathology. Approximately 80% of solid renal masses turned out to be malignant on histopathological examination (HPE).^[1,2] Kidney cancer is the 9th most commonly occurring cancer in men and the 14th most commonly occurring cancer in women.^[3] According to GLOBOCAN 2018, there were around 400,000 new cases reported with renal cancers and among them approximately 90% are renal cell carcinomas (RCC). In comparison to the Asian and African population renal cancers are more frequently seen in the western population ranging from 14.7 to 16.8/lakh population.^[1]

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Renal cancers more frequently are documented than females. in males Abraham et al., from Kochi Kerala, reported an estimated incidence of RCC in males is about 2/100,000 population and in females is about 1/100,000 population.^[4] Other studies also reported male predominance but with early age of occurrence in comparison to western population.^[5,6]

Among various imaging modalities conventionally ultrasonography is the initial investigation of choice. However, it is having a limited role in characterization of small solid renal mass lesions.^[7] Next imaging modality is contrast-enhanced CT (CECT) which is having sensitivity and specificity of around 96% and 78%,

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respectively.^[8] CECT is usually performed for a limited section of body to characterize the mass lesion. However, acquisition of other body sections is separately considered to evaluate distant lesions. There is a definitive role of magnetic resonance imaging (MRI) in differentiating suspected mass lesions such as angiomyolipoma from RCC and other nonenhancing renal tumors based on fat content.^[9]

Often localized renal mass lesion after diagnosis, treated with partial or radical nephrectomy.^[10] In literature, studies documented around 25%–30% of RCC patients are presenting with distant organ metastasis, where chemotherapy, radiotherapy, etc., becomes the mainstay of treatment.^[11,12] Hence, requires proper diagnostic staging before initiation of treatment. Whole-body fluorine18 fluoro-2-deoxy-D-glucose positron emission tomography/ computed tomography (F18-FDG PET/CT) has emerged as an important molecular imaging modality in staging, restaging, recurrence evaluation, and monitoring of therapeutic response in various malignancies in the last two decades. It provides information of both morphological and metabolic characteristics of tumor, locoregional extension, and distant metastases.^[13]

In literature, there are limited data available on F18-FDG PET/CT in renal malignancies, due to its low sensitivity in the detection of primary tumor as high tracer activity in renal pelvis may obscure the tumor detection. However, PET/CT has a potential role to detect distant organ metastases.^[14] Hence, the present study was designed to see the utility of F18-FDG PET/CT in characterization and evaluation of solid renal mass lesions and its impact on treatment planning in the presence or absence of metastatic disease.

Patients and Methods

Twenty-four patients with solid renal mass lesions were included in the study [Table 1]. The study was prospectively performed after obtaining approval from the Institute Thesis Protocol Approval Committee and Institute Ethics Committee. All the patients underwent CECT abdomen prior to PET/CT.

Patient preparation

All patients were prepared following the standard operating procedure guidelines by the Society of Nuclear Medicine

Table 1:	Inclusion	and	exclusion	criteria	of the	study
		p	opulation			

Inclusion criteria	Exclusion criteria
All the patients with CECT	Patients in whom pathological
detected solid renal mass	evaluation (FNAC/biopsy) was done
lesions and treatment naïve	prior to 18F-FDG PET/CT
with age above 18 years	Pregnant women and nursing mothers
Patients willing to	Patients not willing to participate in
participate in the study	the study

CECT: Contrast-enhanced computed tomography, FNAC: Fineneedle aspiration cytology, 18F-FDG PET/CT: F-18 fluorodeoxyglucose positron emission tomography computed tomography and European Association of Nuclear Medicine and Molecular biology in terms of hydration, 6 h of fasting, and oral hypoglycemic medication prior to imaging.^[15,16] F18-FDG was injected only when blood glucose levels were below 160 mg/dl. In case if high blood sugar levels (>160–250 mg/dl) were detected on the day of scan, then those patients were prepared with short-acting insulin protocol.^[17]

Imaging protocol and data acquisition

All F18-FDG PET/CT studies were performed on Biograph-6 (SIEMENS) in a supine position with arms elevated over the head from the skull to mid-thigh after administration of 296–370 MBq (8–10 mCi) [0.14–0.20 mCi/kg] of F18-FDG radiopharmaceutical. After 60 min of F18-FDG administration, initial CT scan was done then followed by PET acquisition. In addition, delayed imaging was done at around 1 h 30 min from early acquisition for all the cases after the administration of loop diuretic (furosemide-dose of 1 mg/Kg) intravenously.

Image processing and analysis

Acquired PET images were corrected using CT attenuation correction map and later PET and CT images were fused using True D and Syngo software. Semi-quantitative analysis of F18-FDG uptake was performed by drawing three-dimensional volume of interest (VOI) over the lesion and maximum standardized uptake value (max.SUV) were obtained.

Max.SUV(cm² / ml)= <u>Radioactivity concentrated in tissue(mCi) / VOI(ml)</u> Injected activity (mCi) / body surface area (cm²)

Interpreting max.SUV of early and delayed images, retention index (RI) was calculated using a formula.

$$RI = \frac{\Delta \text{ Max. SUV} \times 100}{\text{Initial max. SUV}}$$

(\Delta Max.SUV = max.SUV Delayed - max.SUV Initial)

Malignancy was considered quantitatively when max.SUV ≥ 2.5 and RI of $\geq 10\%$. Whereas lesions with max.SUV < 2.5 and RI of < 10% were considered benign. Semi-quantitative max.SUV values and RI of detected lesions were correlated with HPE findings.

Statistical analysis

Considering HPE findings as gold standard, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of F18-FDG PET/CT were calculated. Statistical significance of F18-FDG PET/CT compared to CECT was calculated using McNemar test. P < 0.05 was considered statistically significant. Agreement findings of CECT and F18-FDG PET/CT with HPE were done using Cohen's Kappa coefficient.

Results

Demography and risk factors

The mean age of study group was 53.8 ± 12.3 years with a range of 21–73 years with no statistical significance (P = 0.79) between the age group of males and females in the occurrence of renal malignancy. In the present study group, renal malignancy was predominantly seen in male (M: F-4:1). Patients with renal malignancy were associated with risk factors such as obesity, history of smoking, and alcohol intake [Table 2].

Pathological evaluation

All 24 patients with solid renal mass lesions were histopathologically confirmed either by urine cytology (4.1%) or ultrasound-guided biopsy (20.8%) or postoperative biopsy (75%) after undergoing PET/CT. On HPE, 20/24 (83.3%) renal mass lesions were malignant. Among them, majority are clear cell variant of RCC (ccRCC) (n = 15). Remaining 4/24 lesions were benign on HPE [Table 3].

Fluorine18 fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography findings based on maximum standardized uptake value cut off

Based on max.SUV cut off on PET/CT, all 24 solid renal mass lesions were characterized 17/24 lesions as malignant and remaining 7/24 lesions as benign [Chart 1]. One of the malignant lesions turned out to be xanthogranulomatous pyelonephritis (XGP) on HPE, thus considered as false positive. 4/7 benign lesions proved to be ccRCC on HPE, hence considered as false negative [Figure 1]. Whereas remaining 3/7 benign lesions on PET/CT were remained



Figure 1: (a) MIP image on 18F-FDG PET/CT of 43 years male patient showing (b and c) non FDG avid exophytic heterogeneous soft tissue density mass lesion (white arrows) in axial section involving left kidney upper pole with max.SUV: 2.2 suggestive of benign lesion. Postoperative HPE confirmed the mass lesion as ccRCC. MIP: Maximum intensity projection, PET/CT: Positron emission tomography/computed tomography, HPE: Histopathological examination, ccRCC: Clear cell variant of renal cell carcinomas

as benign on HPE [Figure 2], thus these lesions were considered as true negative [Chart 1]. Mild agreement (Cohen's kappa - 0.423) was seen between findings of F18-FDG PET/CT and HPE. There is a decrease in max. SUV from early to delayed imaging in all histopathological benign lesions. In case of malignant renal lesions on HPE, 50% of lesions showed increasing trend in max. SUV from early to delayed imaging. While remaining 50% lesions (comprising only ccRCC), showed decrease in max.SUV from early to delayed imaging [Table 4]. The

Table 2: Characteristics of study population who
underwent F-18 fluorodeoxyglucose positron emission
tomography computed tomography

Values (mean±SD/range)
18
6
53.4±13.0 (21-73)
55.0±10.8 (45-71)
60.8±11.8 (45-84)
163±12.0 (140-180)
108±12.4 (88-136)
23.0±4.2 (13.3-31.4)
0
2
3
11
1
5
0
2
1
9
0
1
0
5
C C
1
1
1
4
16
10
0
4

SD: Standard deviation, BMI: Body mass index



Chart 1: Characterization of masses based on max.SUV cut off of 2.5. max.SUV: Maximum standardized uptake value

Table 3: Mean of maximum standardized uptake value (early and delayed) of benign and malignant renal lesions				
HPE diagnosis	n	Mean±SD		
		Max.SUV (early)	Max.SUV (delayed)	
Benign (n=4)				
Angiomyolipoma	2	1.7±0.14 (1.6-1.8)	1.2±0.2 (1.1-1.4)	
Xanthogranulomatous pyelonephritis	1	5.8	4.2	
Fibrocollagenous mass	1	1.8	1.2	
Malignant (n=20)				
RCC				
Clear cell RCC	15	5.4±3.8 (2.0-16.2)	5.4±5.2 (1.3-21.4)	
Mucinous tubular and spindle cell RCC	1	8.8	10.3	
Sarcomatoid RCC	1	12.6	17.1	
Primary mucinous adenocarcinoma of renal pelvis	1	2.6	3.0	
Wilms tumor	1	9.8	10.8	
Urothelial carcinoma	1	8.2	11.4	

RCC: Renal cell carcinomas, HPE: Histopathological examination, SD: Standard deviation, Max.SUV: Maximum standardized uptake value

Table 4: Classification of solid renal mass lesions based on retention index				
<10% (n=16)	Angiomyolipoma (<i>n</i> =2)			
	Fibrocollagenous tissue (<i>n</i> =1)			
	Xanthogranulomatous pyelonephritis (n=1)			
	Clear cell RCC (<i>n</i> =12)			
>10% (<i>n</i> =8)	Clear cell RCC (<i>n</i> =3)			
	Mucinous tubular and spindle RCC (n=1)			
	Wilm's tumor (<i>n</i> =1)			
	Primary mucinous adenocarcinoma (n=1)			
	Urothelial carcinoma (n=1)			
	Sarcomatoid RCC (<i>n</i> =1)			

RCC: Renal cell carcinomas, RI: Retention index,

HPE: Histopathological examination

sensitivity, specificity, PPV, NPV, and accuracy of PET/CT were 80%, 75%, 94.1%, 42.8%, and 79.1%, respectively. Statistical significance (P = 0.02) was documented between

max.SUV of overall malignant renal lesions with metastases and without metastases.

Fluorine18 fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography findings based on retention index

For all solid renal mass lesions in 24 patients, RI was calculated. Two-third (16/24) lesions showed RI <10% while remaining one-third (8/24) lesions showed RI ≥10% [Table 4]. No agreement (Cohen's kappa - 0.1818) was seen between HPE findings and RI% values in this study population. The sensitivity, specificity, PPV, NPV, and accuracy of PET/CT findings based on RI were 40%, 100%, 100%, 25%, and 50%, respectively. There was a significant improvement in specificity and PPV PET/CT findings after using RI. However, there was no statistical significance (P = 0.26) between RI of malignant lesions with metastases and without metastases.

Contrast-enhanced computed tomography findings

All 24 patients underwent CECT abdomen prior referring to F18-FDG PET/CT. Based on morphological and enhancement pattern, CECT characterized 20/24 solid renal mass lesions as malignant and remaining 4/24 lesions as benign. 2/20 malignant lesions on CECT turned out to be benign (XGP and fibrocollagenous mass of one each) on HPE, thus considered as false positive. 50% benign lesions were proved to be malignant (ccRCC and primary mucinous adenocarcinoma one each) on HPE, thus considered as a false negative. Mild agreement (Cohen's kappa –0.400) was documented between F18-FDG PET/CT and CECT abdomen findings.

Staging of malignant renal lesions

Tumor staging

On CECT abdomen, 18/20 (90%) malignant renal lesions are true positive. While on F18-FDG PET/CT, 16/17 (94%) malignant renal lesions are true positive. Table 5 describes

Table 5: Stage migration post F-18 fluorodeoxyglucose positron emission tomography computed tomography						
Pre 18F-FDG PET/CT stage	<i>n</i> =24	Post 18F-FDG PET/CT staging				Upstaging, n (%)
		Ι	II	III	IV	
Ι	8	4	0	0	3+1*	4 (50)
II	3	0	3	0	0	-
III	5	0	0	4	1	1 (20)
IV	4	0	0	0	4	-
Total	20	4	3	4	9	5 (25)

*RCC with only supraclavicular lymph node involvement. RCC: Renal cell carcinomas, 18F-FDG PET/CT: F-18 fluorodeoxyglucose positron emission tomography computed tomography



Figure 2: (a) MIP image on F18-FDG PET/CT of a 45 years female patient showing (b and c) non-FDG avid ill-defined heterogenous soft tissue density mass lesion (white arrows) in axial section with areas of fat attenuation involving upper pole of left kidney with max.SUV: 1.6, suggestive of benign lesion. Postoperative HPE confirmed the mass lesion as angiomyolipoma. MIP: Maximum intensity projection, F18-FDG: Fluorine18 Fluoro-2-deoxy-D-glucose, PET/CT: Positron emission tomography/ computed tomography, HPE: Histopathological examination, ccRCC: Clear cell variant of renal cell carcinomas

the tumor staging on F18-FDG PET/CT in comparison with CECT abdomen. The mean size of lesion at the primary site was 10.0 ± 6.9 cm and 9.8 ± 6.8 cm on CECT and F18-FDG PET/CT, respectively.

Regional lymph nodal involvement on fluorine18 fluoro-2-deoxy-D-glucose positron emission tomography/ computed tomography

Among the HPE-proven renal lesions, F18-FDG PET/CT detected regional lymph nodal involvement in 5/20 patients. Whereas on CECT, 6/20 patients showed regional node involvement.

Nonregional lymph nodal involvement on fluorine18 fluoro-2-deoxy-D-glucose positron emission tomography/ computed tomography

In addition to the regional lymph nodes, PET/CT also localized nonregional lymph nodes in 6/20 (30%) patients. One patient with a malignant renal lesion showed supraclavicular lymph nodes as only site of involvement, thus considered as case of distant metastases.

Distant organ involvement

In our study, PET/CT whole-body survey documented distant organ metastases in 8/20 (40%) patients. Among them, 4/8 patients were having two or more organ involvement which includes brain, liver, lung, bone, muscle, and adrenal gland [Figure 3]. While the remaining 4/8 patients showed single organ involvement [Table 5].

Discussion

Renal malignancies tend to occur in a relatively early age in Asian and African population as compared to western population.^[1] The same was observed in Indian studies. Joshi *et al.* documented that the median age of RCC was 56.6 years.^[5,6] In the present study, we also observed a similar early occurrence of RCC with the median age of 56 years, which is earlier in comparison to western population at 6th-7th decade.

In literature, renal malignancies showed male preponderance. Hew *et al.*, in a retrospective study from the Netherlands, observed M: F ratio of $2:1.^{[18]}$ Whereas in a Indian study by Tiwari *et al.*, M: F was $3.5:1.^{[19]}$ A similar finding was noted in our study with M: F ratio of 4:1.

In a meta-analysis, Chow *et al.* evaluated the risk factors related with the occurrence of renal malignancies.^[20] They observed that smoking, obesity, etc., were predominantly associated risk factors. The same was observed in our study. 9/20 (55%) had a history of smoking alone while 5/20 (25%) had a history of both smoking and alcoholism. 7/20 (35%) patients with malignancy were with BMI >25 kg/m².

Histologically, about 90% of total renal malignancies will be comprising of RCC only.^[1] Similarly, we observed



Figure 3: (a) MIP image on F18-FDG PET/CT images of a 47 years male patient showing (b and c) soft tissue density mass lesion in axial section involving left kidney lower pole with max.SUV: 3.7 (White arrow) suggestive of malignant lesion. Postoperative HPE confirmed the mass lesion as ccRCC. (d and e) Images showing mild increased FDG concentration in isodense lesion with central hypodensity in right parieto-occipital region (red arrows) with disproportionate edema s/o brain metastases. MIP: Maximum intensity projection, F18-FDG: Fluorine18 fluoro-2-deoxy-D-glucose, PET/CT: Positron emission tomography/computed tomography, max.SUV: Maximum standardized uptake value, HPE: Histopathological examination, ccRCC: Clear cell variant of renal cell carcinomas

17/20 (85%) renal lesions were RCC. While remaining 3/20 (15%) lesions include Wilms tumor, primary mucinous adenocarcinoma of renal pelvis, and urothelial carcinoma, respectively.

Currently available evidence suggests that both CECT and contrast-enhanced MRI (CEMR) are considered to be the gold standard in the characterization of solid renal mass lesions. In a systematic review, Furrer *et al.*, from Switzerland, reported the sensitivity and specificity of CECT and CEMR of 96% and 78%, 77%, and 75%, respectively.^[21]

Wang *et al.*, from Taiwan, performed a meta-analysis and reported a pooled sensitivity and specificity of F18-FDG PET in the detection of renal malignancy are 62% and 88%, respectively.^[22] Whereas in our study, sensitivity and specificity were 80% and 75%, respectively. Better sensitivity in our study could be due to adopted low cut-off max.SUV. While using the RI \geq 10%, we observed improvement in specificity from 75% to 100% and PPV from 94% to 100%.

We observed, 4/7 (57%) benign renal lesions on PET/ CT, confirmed as ccRCC on HPE thus considered as false negative. These lesions showed max.SUV below 2.5 and RI <10%. Various studies on ccRCC documented, varied expression of Fructose 1,6-bisphosphatase 1, hexokinase 2, and glucose transporter 1 may result in lower FDG uptake.^[23] This may be a reason for lower FDG uptake in our study.

All non-RCC renal lesions were showing high max.SUV and RI \geq 10% except Primary mucinous adenocarcinoma of renal pelvis which showed relatively lower max.SUV of 2.6. The lower max.SUV may be possibly due to low cellular density and high mucinous content of the tumor tissue [Figure 2].^[24] This could be one of the reasons for lower sensitivity of 18F-FDG PET/CT in comparison to the CECT and CEMRI.

1/17 malignant renal lesion on PET/CT with max.SUV of 5.8 turned out to be XGP on HPE, thus considered as false positive. A study has been documented the possibility of miss-diagnosing a case of XGP as malignant depending on the absence of fat stranding and diffuse FDG uptake.^[25]

CECT abdomen showed regional lymph node positivity in 6/20 (30%) patients with malignant renal lesions. Whereas PET/CT localized regional lymph nodes in 5/20 (25%) patients which were due to size <1 cm. Supporting to our finding, a study by Ozkan *et al.*, from Turkey in 22 RCC patients with lymph node size <1 cm showed lower sensitivity of PET system because of poor resolution.^[26]

In our study group, PET/CT detected distant metastases in 9/20 (45%) patients. 8/9 patients were associated with distant organ (liver, lung, brain, adrenal gland, and muscle) involvement. 1/9 patients had supraclavicular lymph node as only site of involvement thus considered as distant metastases. Among them, 4/8 (50%) of patients were with multi-organ metastases. Remaining 4/8 (50%) patients were with single organ metastases. The involvement of bone is seen in 4/8 (50%), liver in 4/8 (50%), lung in 3/8 (37.5%), brain in 2/8 (25%), adrenal gland in 2/8 (25%), and muscle in 1/8 (12.5%) patients. Similar to our findings, a large study by Bianchi *et al.*, in 11,157 RCC patients with distant metastases documented involvement of lung (45.2%), bone (29.5%), liver (20.3%), adrenal gland (8.9%), and brain (8.1%) of patients.^[27]

F18-FDG PET/CT is well established for staging, treatment response evaluation, and detection of recurrence for various cancers in the body. Park *et al.*, in 63 patients of RCC in postoperative setting using PET/CT, reported 11/63 patients positive for recurrence and 33/63 patients positive for distant organ metastases.^[28] In another study by Sivaramakrishna *et al.*, 50% of RCC patients after surgery were positive for distant metastases involving lung, bone, brain, and supraclavicular nodes detected in various conventional imaging modalities such as USG, CXR, CECT, and bone scan which could not be picked up by initial CECT abdomen.^[29] Thus, considering the importance of diagnostic systematic whole-body survey and limited data on solid renal mass lesions, the current study was performed.

In the current study, CECT detected metastatic disease in 4/20 patients in limited abdominal section imaging not intended for metastatic disease evaluation on initial workup. While PET/CT whole-body imaging in our study localized distant metastatic sites additionally in 5/20 (25%). In literature, a similar type of studies in RCC patients reported advantage of PET/CT whole-body survey by localizing additional sites of metastases ranging from 5.7% to 30%.^[14,30]

Change in management

In the current urology practice, CECT is the standard of care imaging modality for diagnosis and treatment planning in patients presented with renal masses. In an F18-FDG PET CT-based study, Kumar *et al.* evaluated 28 patients of solid renal masses and reported change in management in 30% of cases.^[31] Similarly, the current study also showed change in management in additional 5/20 (25%) patients, who were characterized as malignant mass lesion with metastases.

Tumor prognostication

The intensity of F18-FDG concentration in various primary cancers is often used for prognostication. In a study from South Korea, Lee *et al.* evaluated 23 RCC patients and observed the mean of max.SUV values were 5.3 ± 1.7 and 2.9 ± 1.0 in patients with and without metastasis, respectively, with P < 0.05.^[32] In our study group, we also observed the similar difference in mean of max.SUV values of 8.3 ± 4.6 and 4.1 ± 2.1 among patients with and without distant metastasis, respectively, with P = 0.02 (<0.5) which was statistically significant.

Limitations of our study are small sample size, histopathological grading, and max.SUV of renal mass lesions were not correlated and finally multicentricity of the study with large sample size is required to validate the results.

Conclusion

A cut-off value of max.SUV of 2.5 from F18-FDG PET/CT can characterize solid renal masses with reasonably high specificity. However, needs careful consideration of other parameters (RI) obtained from dual-time-point imaging. F18-FDG PET/CT whole-body scan can additionally provide distant site involvement at the time of mass characterization at initial staging. Thus helps in planning of optimal treatment.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initial s will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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