Review Article

Dimercaptosuccinic acid: A multifunctional cost effective agent for imaging and therapy

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ABSTRACT

Dimercaptosuccinic acid (DMSA) is an analog of dimercaprol used as metal chelating moiety in variety of conditions. In nuclear medicine itself two types of Tc-99m DMSA complexes are used, trivalent and pentavalent forms. In this review, we have discussed the mechanism of uptake of both complexes as well as diagnostic and therapeutic application in a clinical scenario.

Keywords: Dimercaptosuccinic acid, glucose-mediated acidosis, pentavalent, renal cortex, trivalent

INTRODUCTION

Dimercaptosuccinic acid (DMSA) contains two sulfhydryl groups, an analog of dimercaprol and is used for metal chelation. Traditionally, this has been used as an antidote to heavy metal toxicity.[1,2] It is also reported to be used for removal of heavy metals from the body of autistic children, a one major concern in autism.[3] However, its chelation property has been exploited in nuclear medicine. Tc-99m labeled DMSA shows altered organ distribution depending on methods of preparation. At acidic pH (pH 2–3), DMSA chelates with technetium in lower oxidation (III) and forms a trivalent complex Tc-99m (III) DMSA also represented as Tc-99m DMSA [Figure 1a]. Tc-99m DMSA accumulates in proximal tubular cells of kidneys and thereby used for renal cortical imaging. At alkaline pH (pH 8–9), it chelates with technetium in higher oxidation state to form a pentavalent complex Tc-99m (V) DMSA, resembles phosphate ion and is rapidly excreted in the urine[4] [Figure 1b].

MECHANISM OF UPTAKE

Trivalent Tc-99m dimercaptosuccinic acid

Trivalent Tc-99m DMSA has high binding affinity for the proximal convoluted tubules thus providing good imaging of the renal parenchyma. Two main Tc-99m DMSA tubular uptake routes have been proposed (i) peritubular extraction from plasma and (ii) tubular reabsorption.[5,6] Muller and Gutsche in 1995 proposed that after injection, Tc-99m DMSA is bound to plasma proteins in the circulating blood and penetrate the glomerular filter at very low rates. Tc-99m DMSA is completely excreted and does not reabsorbed from the tubular fluid. Peritubular excretion accounts for the Tc-99m DMSA uptake in the proximal tubular cells of the renal cortex. Tc-99m DMSA is then bound to the cell plasma protein with a high binding constant and accumulates in the kidney.[6] Burckhardt *et al.* proposed the role of sodium-dependent dicarboxylate transporter (NaDC-3) in the basolateral uptake of Tc-99m DMSA from peritubular capillaries into proximal tubule cells.[7] Tc-99m DMSA reabsorption from the glomerular ultra-filtrate substantially contributes to the renal uptake of the tracer.[8-10] Recently, Weyer *et al.* studied the role of the megalin/cubilin receptors for the accumulation of Tc-99m DMSA and proposed that Tc-99m DMSA binds to α-1 microglobulin plasma protein. Tc-99m DMSA is freely filtered by glomeruli and accumulates in renal proximal tubules by multiligand-binding mediated by megalin/cubilin receptor endocytosis. Free Tc-99m DMSA and trace amounts of microglobulin–bound Tc-99m DMSA are excreted in the urine.[11]

Pentavalent Tc-99m (V) dimercaptosuccinic acid

Tc-99m (V) DMSA localizes in a number of tumor types, most notably medullary thyroid carcinoma (MTC), bone metastases and other bone lesions. At pentavalent state, both sulfhydryl groups (-SH) of DMSA are bound with Tc-99m and no free -SH group is left for protein binding [Figure 1b]. The small Tc-99m (V) DMSA complex does not accumulate in the kidney and gets easily excreted by the kidney.[12]

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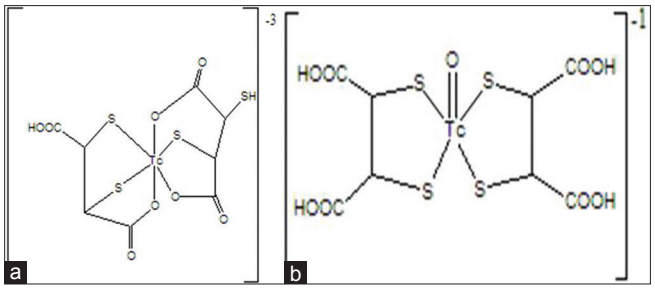

Figure 1: Chemical structure of (a) Tc-99m (III) dimercaptosuccinic acid (DMSA) and (b) Tc-99m (V) DMSA

Tc-99m (V) DMSA core has structural similarity with phosphate ion (PO_4^{-3}) and is avidly taken up by metabolic active cancer cells.[13,14] In addition, Tc-99m (V) DMSA uptake by tumors is related to glucose-mediated acidosis and mitotic activity.[15,16] In aggressive or malignant tumors the rate of glycolysis, so the production of lactic acid is increased that results in the acidic pH of the tumor microenvironment.[17,18] Phosphate is transported via all three NaPi co-transporters, however, Tc-99m (V) DMSA is transported by NaPi Type III co-transporters and can be used as a tumor proliferation marker.[19] Physiological uptake of Tc-99m (V) DMSA has been reported in the nasal mucosa, lacrimal glands and blood pool such as in the heart, and vessels. The excretion of Tc-99m(V)DMSA is through kidney. Uptake is also noted in pituitary and breast.[20,21]

FACTORS INFLUENCING THE UPTAKE OF TC-99m (V) DMSA

Phosphonoformic acid

The phosphate accumulation is linked to NaPi Type III co-transporter expression In the presence of a specific NaPi cotransporter inhibitor, phosphonoformic acid, Tc-99m (V) DMSA accumulation decreases with the decreased phosphate accumulation.[19]

Extracellular sodium concentration

Tc-99m (V) DMSA uptake is dependent on extracellular sodium concentration, in the same way as phosphate uptake, suggesting an important role of sodium-dependent transporter in Tc-99m (V) DMSA uptake and more specifically, the involvement of NaPi co-transporter, as phosphate transporters is known to be strongly dependent on extracellular sodium.[22] In the absence of extracellular sodium only <30% Tc-99m (V) DMSA enters in cells by simple diffusion.

pH

Uptake of both Tc-99m (V) DMSA and phosphate is stimulated at acidic pH and inhibited at alkaline pH. The plausible reason is that at acidic pH, carboxyl groups of DMSA (V) are fully associated and impart an average global charge of −1 to the DMSA (V) complex. The activity of Type III NaPi co-transporters increases because of preference for monovalent substrates.[18,23] Tumor cells over express Type III NaPi co-transporters and have more acidic extracellular pH than normal tissues.[15,17]

Applications of dimercaptosuccinic acid in nuclear medicine

Dimercaptosuccinic acid is a very useful radiopharmaceutical and being used for the detection of many diseases such as renal disorder, MTC, brain tumor, etc. Pentavalent Re-188/Re-186 DMSA is suitable candidate for internal radiation therapy.

TRIVALENT DIMERCAPTOSUCCINIC ACID (Tc-99m DMSA)

Renal disorders

At low pH (2–3), trivalent Tc-99m DMSA is formed and localizes in the kidney. Since it is taken up by renal cortex and retained there, according to latest EANM guidelines, trivalent Tc-99m DMSA is the agent of choice for the detection of focal renal parenchymal abnormalities, renal sequelae after acute infection, acute pyelonephritis, ectopic kidney, confirmation of nonfunctional multicystic kidney and associated abnormalities such as abnormal duplex kidney, small kidney, dysplastic tissue, horseshoe kidney etc.[24] It is very useful in the detection of renal cortical scars. The superior renal to background ratio offered by DMSA is useful in the diagnosis of congenital renal conditions such as horseshoe kidney, ectopic kidney, crossed fused ectopic kidney. Tc-99m DMSA is also used to evaluate kidney parenchyma, functioning renal tissue and proximal tubular dysfunction. This scintigraphy has a great value in the diagnosis and evaluation of tubule-interstitial nephropathy in diseases like Joubert syndrome.[25]

Tc-99m DMSA renal scintigraphy can also be used to assess effects of cytotoxic drugs such as ifosfamide, cisplatin, methotrexate and cyclophosphamide on renal function in children who receive chemotherapy for various malignancies. A highly significant relationship has been reported between Tc-99m DMSA uptake and cumulative ifosfamide dose ($P < 0.001$).[26] Tc-99m DMSA scintigraphy is a noninvasive and sensitive method for the detection of ifosfamide-induced tubular dysfunction, subclinical injury and to predict risk at retreatment.[26-28]

PENTAVALENT DIMERCAPTOSUCCINIC ACID (Tc-99m (V) DMSA)

The blood pool activity of Tc-99m (V) DMSA is seen up to 3 h and is actively taken up by the growing bones. Tc-99m (V) DMSA is proved to be useful in patients with MTC, brain, and soft tissue tumors. However in lung, liver, gastrointestinal tract, malignant melanoma and lymphoma Tc-99m (V) DMSA has only limited role.[29] The biodistribution and diagnostic value of Tc-99m (V) DMSA planar and single photon emission computed tomography (SPECT) scintigraphy had been assessed in patients with head and neck tumors. The results showed the bi-exponential blood clearance and rapid elimination from all organs except kidneys.[30]

Medullary carcinoma of thyroid

Medullary carcinoma of the thyroid is an uncommon tumor and arises from the parafollicular cells of the thyroid. The early detection of tumor sites in patients with MTC is important as it tends to metastasize to regional neck lymph nodes and mediastinum.[31] The major distant metastasis sites are lung, liver, and bones. Tc-99m (V) DMSA has demonstrated to be taken up by the primary as well as recurrent and metastatic tumors[32-35] [Table 1]. Intense accumulation of Tc-99m (V) DMSA is found in MTC and its metastatic sites.[36] Tc-99m (V) DMSA is found to be very specific since no significant uptake is observed in other thyroid malignancies, normal thyroid, salivary glands, and bones.[37]

Tc-99m (V) DMSA has been compared to Tc-99m tetrofosmin and Tl-201 in patients of MTC with variable calcitonin levels and showed superior detection of metastatic sites in patients with MTC over Tc-99m tetrofosmin and Tl-201 scintigraphy.[35] Tc-99m (V) DMSA showed sensitivity similar to In-111 octreotide and I-131 MIBG in localizing primary MTC; but, these scans are unable to detect small lymph node involvement before initial surgery.[37,38] However, the sensitivity may improve with high serum calcitonin levels[39,40] Tc-99m (V) DMSA demonstrated better sensitivity and specificity as compared to CT and can be used for identification of recurrence or metastasis of MTC.[40,41] In another study based on the lesion sensitivity, Tc-99m (V) DMSA has been found to be superior to Tc-99m MIBI and Tl-201in the follow-up of MTC patients.[42] Tc-99m (V) DMSA may result in early diagnosis and proper management of patients with MTC [Table 1].

Head and neck

The identification of primary and metastatic sites plays an important role in the treatment and management of squamous cell carcinoma (SCC). Many radiopharmaceuticals such as Ga-67 citrate, Co-57 bleomycin, In-111 bleomycin, etc. have been used in past with low sensitivity and specificity. The studies of head and neck SCC of Tc-99m DMSA showed good uptake at the primary tumor and correlated well with the results of clinical and conventional imaging findings. However, it is found to be less sensitive for metastatic cervical nodes.[43-45] Tc-99m (V) DMSA SPECT imaging demonstrated high affinity in patients with oral SCC for metastatic lymph nodes in the neck and were helpful for designing proper neck dissection.[46,47] Tc-99m (V) DMSA showed no role in detecting primary nasopharyngeal carcinoma (NPC).[48,49] However, metastatic neck lymph node lesions of NPC could be detected by Tc-99m (V) DMSA. These studies demonstrated that Tc-99m (V) DMSA imaging may be used for the detection of the primary site in SCC of head and neck, with limited utility in the evaluation of cervical nodes.[45] The role of Tc-99m (V) DMSA has been explored in other head and neck malignancies like pharyngolaryngeal carcinoma and parotid tumors and fairly good results were obtained[30,50] [Table 2].

Ocular tumors

Tc-99m (V) DMSA scintigraphy may play a crucial role in the detection and follow-up of retinoblastoma, uveal amelanotic melanoma, and choroidal melanoma. Locally extended as well as a metastatic orbital retinoblastoma has been assessed by Tc-99m (V) DMSA. Planar and SPECT images demonstrated primary and metastatic sites which were confirmed by ultrasonography, magnetic resonance imaging, and incision biopsy.[51] Intraocular tumor of metastatic breast, lung, and rectal carcinomas can be imaged by Tc-99m (V) DMSA. The scan also detected unknown primary and other systemic lesions that may help in the diagnosis and the management of these patients[52-54] [Table 2]. This group suggested the complementary role of Tc-99m (V) DMSA on rare situations of decision making.

Brain tumors

Tc-99m (V) DMSA can be used as a promising agent for brain tumors. It has high specificity for differential diagnosis of benign from malignant tumors and also differentiating their histological malignancy grade, noninvasively. Approximately 95% of benign and malignant primary brain tumors are detected by Tc-99m (V) DMSA SPECT images. The vascularity could be adjudged by early uptake ratios without statistically significant difference in

Table 1: Studies showing role of Tc-99m (V) DMSA in MTC

Authors year	Number of patients	Tumor	Sensitivity/specificity	Gold standard/compared with	Reference number
Kurtaran *et al.*, 1998	22	MTC	(58%) primary (36%) metastatic	Histopathology, histochemistry	[31]
Clarke *et al.*, 1987	10	MTC	80%	Biopsy (histology)	[32]
Clarke *et al.*, 1988	9	MTC	95%	Histology	[33]
Clarke *et al.*, 1989	32	MTC	80%	Histology	[34]
Adalet *et al.*, 1999	24	MTC	88% (TP)	TI-201, Tc-99m tetrofosmin	[35]
Ohta *et al.*, 1984	4	MTC	-	-	[36]
Berná *et al.*, 1995	11	MTC	8 sites in 5/11 9 sites in 6/11 (In)	In-111 octreotide	[37]
Guerra *et al.*, 1989	26	MTC	84%	I-131 MIBG	[38]
Mojiminiyi *et al.*, 1991	10	MTC	-	Serum calcitonin	[39]
Arslan *et al.*, 2001	14	MTC	57% with octreotide 85%	CT/MRI	[40]
Dabiri 2006	15	MTC	91%, 75%	Serum calcitonin	[41]
Ugur *et al.*, 1996	14	Recurrent MTC	95%	CT/MRI TI-201, Tc-99m MIBI	[42]

DMSA: Dimercaptosuccinic acid, MTC: Medullary thyroid carcinoma, MRI: Magnetic resonance imaging, CT: Computed tomography, MIBI: 2-methoxyisobutylisonitrile

Table 2: Studies showing role of Tc-99m (V) DMSA in head and neck, ocular and brain tumors

Authors year	Number of patients	Tumor	Sensitivity/specificity	Gold standard/compared with	Reference number
Watkinson *et al.*, 1989	62	Head and neck	85%/78%	Histopathology	[43]
Watkinson *et al.*, 1991	26	Head and neck	48%	CT	[44]
Heinritz *et al.*, 1992	17	Head and neck	-	Biopsy	[45]
Zhang *et al.*, 2004	32	SCC (oral cavity)	75.0%/90.0%	Histopathology	[46]
Ohta *et al.*, 1985	76	Head and neck	85%	Histopathology	[47]
Kao *et al.*, 1993	27	Head and neck Nasopharynx	Poor	Biopsy	[48]
Aw *et al.*, 1986	18	Nasopharyngeal carcinoma	28%		[49]
An *et al.*, 2000	20	Head and neck (pharyngolaryngeal carcinoma)	77%/71% primary 75%/100% lymphadenmetastases	Histology	[30]
Wu *et al.*, 1999	45	Head and neck Parotid lump	93%/72%	Ultrasonography, pathology	[50]
Kiratli *et al.*, 1998	12	Choroidal melanoma detection and response	Response evaluation	-	[51]
Kiratli *et al.*, 1998	1	Orbital retinoblastoma	-	Ultrasonography, biopsy, MRI	[52]
Kiratli *et al.*, 1998	3	Metastatic intraocular tumors	-	-	[53]
Kiratli *et al.*, 1997	1	Uveal amelanotic melanoma	-	Ultrasonography, MRI	[54]
Hirano *et al.*, 1997	100	Brain	93% primary 88% metastasis	Tl-201Cl, MRI/CT	[55]
Hirano *et al.*, 1997	57	Brain	95%	Histology, malignancy grade	[56]
Lastoria *et al.*, 1995	53	Pituitary adenomas	81% Accurate response evaluation	Biochemistry	[57]
Yamamura *et al.*, 2003	21	Pituitary adenomas	81%		[58]
Colao *et al.*, 2002	31	Pituitary adenomas	NFA-72% GH-secreting-72% PRL secreting-100%	CT/MRI	[59]
Tsiouris *et al.*, 2007	1	GBM (recurrence)	Response to imatinib therapy	*In vivo*/*In vitro* mounting	[60]

MRI: Magnetic resonance imaging, CT: Computed tomography, DMSA: Dimercaptosuccinic acid, NFA: Nonfunctioning pituitary adenomas, GH: Growth hormone, PRL: Prolactin, GBM: Glioblastoma multiforme, SCC: Squamous cell carcinoma

the tumor histology. The delayed uptake ratio, retention ratio, and retention index are higher for the malignant tumors as compared to the benign pathology. Tc-99m (V) DMSA also demonstrated superiority over Tl-201 imaging for primary and metastatic brain tumors[55-60] [Table 2].

Lung carcinoma

Role of Tc-99m (V) DMSA has also been assessed in primary lung cancers and related bone metastases. Various types of primary lung cancers (adenocarcinoma, SCC, small-cell carcinoma, large-cell carcinoma and bronchial carcinoid tumor) could also be detected (~90%) by Tc-99m (V) DMSA SPECT. No false-positive case for the primary lesions was reported. Uptake ratios were higher in SCCs than adenocarcinomas.[61-64] However, evaluation of mediastinal tumor extension and nodal metastatic lesions are difficult due to the high blood-pool activity and slow cardiovascular clearance. Differentiation of lung cancer from single solid lung mass showed little importance of Tc-99m (V) DMSA [Table 3].

Soft tissue tumor

Tc-99m (V) DMSA demonstrated diagnostic potential in histological proven cases of soft tissue tumors. Tc-99m (V) DMSA uptake is observed in almost all sarcomas, metastatic carcinomas, highly recurrent benign tumors of extra-abdominal desmoids, tenosynovial giant cell tumors, hemangiomas, and granulomatous soft-tissue lesions. Low-grade malignant and highly recurrent benign lesions can be detected with Tc-99m (V) DMSA scintigraphy with no uptake in benign solid soft tissue tumors[65,66] [Table 3].

Breast cancer

The role of Tc-99m (V) DMSA has been explored in scintimammography and demonstrated high sensitivity and specificity for breast cancers patients with high T/B ratios. Tc-99m (V) DMSA could detect cases of nonpalpable ductal carcinoma *in situ*, metastatic lymph nodes and preinvasive lesions with risk of developing malignancy. It is suitable for the assessment of primary lesions and axillary involvement in breast cancer patients and also for the surgical planning of such patients.[67-70] The uptake of Tc-99m (V) DMSA is found to have a positive correlation with the proliferative activity (Ki-67) of breast cancer cells. Tc-99m (V) DMSA uptake in breast cancer and Ki-67 expression suggests Tc-99m (V) DMSA as a surrogate marker of cell proliferation.[71] Tc-99m (V) DMSA correlates with tumor aggressiveness and provides important information regarding the correlation of tumor subtype with breast density[72] [Table 4].

Skeletal metastases

Tc-99m (V) DMSA has also been evaluated in the detection of metastatic and degenerative bone lesions. The diagnostic efficacy of Tc-99m (V) DMSA in the detection of bone metastases is comparable to Tc-99m-methylene diphosphonate (MDP).

Table 3: Studies showing role of Tc-99m (V) DMSA in lung, soft tissue and breast cancers

Authors year	Number of patients	Tumor	Sensitivity/specificity	Gold standard/ compared with	Reference number
Hirano *et al.*, 1995	31	Lung	90%	-	[61]
Kao *et al.*, 1992	50	Lung	43%/70%	X-ray	[62]
Atasever *et al.*, 1997	36	Lung	90%	Clinical/radiological	[63]
Ergün *et al.*, 2007	12	Lung	90%	Tc-99m MDP	[64]
Kobayashi *et al.*, 1993	3	Tenosynovial giant tumor	100%	Ga-67 citrate	[65]
Kobayashi *et al.*, 1994	76	Soft tissue tumor	~100%	Histology, Ga-67 citrate	[66]
Papantoniou *et al.*, 2000	41	Breast cancer	88%/93% breast cancer 78%/86% lymph node metastasis	Mammogram Sestamibi	[67]
Massardo *et al.*, 2002	111	Breast cancer	Sensitivity 7.4% and/100%-Axillary lymph nodes Specificity 100%	Sestamibi, histology	[68]
Papantoniou *et al.*, 2002	45	Breast cancer	92.5%	Sestamibi	[69]
Ambrus *et al.*, 1997	51	Breast cancer	53%/95% Scintimammography	Tc-99m MIBI Scintimammography, ultrasonography	[70]
Papantoniou *et al.*, 2004	34	Breast cancer	-	Ki-67	[71]
Papantoniou *et al.*, 2011	55	Breast cancer in dense breast	-	Histology, mammography	[72]

DMSA: Dimercaptosuccinic acid, MDP: Methylene diphosphonate, MIBI: 2-methoxyisobutylisonitrile

Table 4: Studies showing role of Tc-99m (V) DMSA in skeletal cancers (primary and metastatic) other cancers, infections and response to therapy

Author, year	Number of patients	Pathology	Sensitivity/specificity	Gold standard/compared with	Reference number
Kobayashi *et al.*, 1995	17	Chondrogenic	44% benign 100% malignant	Histopathology	[73]
Ugur *et al.*, 1996	14 (MTC)	Bone metastases	95%/100%	Tc-99m MIBI Tl-201	[42]
Lam *et al.*, 1997	10	Bone metastasis	86%	Tc-99m HDP	[74]
Sahin *et al.*, 2000	34	Bone metastasis	90%	Tc-99m MDP	[75]
Zissimopoulos *et al.*, 2005	28	Osteosarcoma/ osteomyelitis/bone fractures	100%	FNA, Tc-99m MDP, CT	[76]
Choong *et al.*, 2004	92	Cartilaginous tumors	-	Histological examination, Tl-201	[77]
Bandopadhyaya *et al.*, 2012	22	Osteosarcoma	100% primary and metastatic lesions >1 cm	F-18FDG-PET	[78]
Basu *et al.*, 2004	17	Skeletal metastases		Tc-99m MDP	[79]
Wang *et al.*, 1999	9	HCC	88.9%	X-ray/CT	[80]
Banci *et al.*, 1996	5	Pancreatic NET	100%	Histologic/cytologic	[81]
Lee *et al.*, 2001	62	Intestinal inflammation	95%/94%	Colonoscopy/biopsy	[82]
Koutroubakis *et al.*, 2003	76	IBD	92%/86%	Endoscopic and histology	[83]
Javadi *et al.*, 2013	54	IBD	-	Colonoscopy Good correlation	[84]
Lee *et al.*, 1998	36	Bone and joint infection	-	Ga-67 citrate	[85]
Akbunar *et al.*, 2000	8	Metabolic bone disease	86%	Biochemical evaluation	[86]
Ohta *et al.*, 1990	11	Fibromatosis	100%	Histology	[87]
Kobayashi *et al.*, 1994	3	Granulomatous sarcoidosis	100%	CT/MRI/Ga-67 citrate, histology	[88]
Sarikaya al., 2002	11	Renal osteodystrophy	100% D_3 therapy response	Biochemistry	[89]
Koutsikos *et al.*, 2005	20	Multiple myeloma	Response to chemo-therapy	Tc-99m MIBI	[90]

DMSA: Dimercaptosuccinic acid, MTC: Medullary thyroid carcinoma, HCC: Hepatocellular carcinoma, NET: Neuroendocrine tumors, IBD: Inflammatory bowel disease, MIBI: 2-methoxyisobutylisonitrile, MDP: Methylene diphosphonate, CT: Computed tomography, MRI: Magnetic resonance imaging, FNA: Fine needle aspiration

However, degenerative lesions do not show the uptake of Tc-99m (V) DMSA.[42,73-76] Choong *et al.* evaluated Tc-99m (V) DMSA and Tl-201 imaging in the management of cartilaginous tumors and compared with histology.[77] Tc-99m (V) DMSA SPECT/CT in patients with osteosarcoma is found to be comparable with F-18 fluorodeoxyglucose (F-18 FDG) PET/CT in the evaluation of primary and metastatic lesions with size more than 1cm. However, F-18-FDG PET/CT could also detect sub-centimeter lesions.[78] Basu *et al.* studied and compared the findings of Tc-99m-MDP bone scan and Tc-99m (V) DMSA scintigraphy in the detection of osseous metastases arising from various malignancies[79] [Table 4].

Other tumors

The role of Tc-99m (V) DMSA has not been established in patients with carcinomas of the gastrointestinal tract, malignant melanoma, and lymphoma.[28] However, one study demonstrated approximately 90% sensitivity of Tc-99m (V) DMSA in the detection of hepatocellular carcinoma.[80] Pancreatic neuroendocrine tumors also demonstrated high uptake of Tc-99m (V) DMSA[81] [Table 4].

Infection and inflammation

Tc-99m (V) DMSA is also evaluated as an agent for visualization of inflammatory lesions and proven as a procedure of choice with colonoscopy for confirming the diagnosis.[82-84] Tc-99m (V) DMSA showed greater sensitivity and as well as accuracy than Ga-67 in the assessment of bone and joint infection, metabolic bone disease. However, the difference is not statistically significant.[85,86] High uptake at the sites of fibromatosis and moderate uptake at granulomatous inflammatory lesions of sarcoidosis is shown with Tc-99m (V) DMSA and could be of value in the diagnosis and in determining the appropriate site for biopsy[87,88] [Table 3].

Therapy and response evaluation

Re-186/188 (V) DMSA is a therapeutic analog of Tc-99m (V) DMSA and may be used for therapy of soft tissue tumors and bony metastases.[74] Basu *et al.* demonstrated the role a Tc-99m (V) DMSA in selection of patients for Re-188 (V) DMSA therapy and response evaluation to bisphosphonate therapy.[79] Re-186/188 (V) DMSA offers the potential for targeted radiotherapy, the avidity of the tracer in most bone metastasis suggests that this could be applied for palliative treatment. Tc-99m (V) DMSA is a noninvasive tumor cell proliferation marker and may also be used to evaluate the response to radio and chemotherapy, predict patient prognosis and help in management of various tumors and other therapies.[51,60,89,90]

CONCLUSION

Trivalent Tc-99m DMSA is a widely used tracer for renal cortical imaging. Tc-99m (V) DMSA accumulation is linked to phosphate uptake and kinase pathway activation and act as a surrogate marker of cell proliferation. It has the potential role in patient management, prognosis estimation, and therapy response monitoring. However, sensitivity is not comparable to F-18-FDG PET/CT in the detection of sub-centimeter nodules due to lower spatial resolution of the gamma camera than the PET/CT. The cost of F-18-FDG PET/CT scan is many times more than the cost of a Tc-99m (V) DMSA scan. However, it seems to be a good alternate to F-18-FDG PET/CT in those centers where PET/CT is not available. Furthermore, the sensitivity of Tc-99m (V) DMSA scan may be improved for detection of sub-centimeter nodules using the SPECT/CT. The β-emitting analogs Re-186/188 (V) DMSA offers the potential for targeted radiotherapy to Tc-99m (V) DMSA avid bone metastasis for palliative treatment.

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