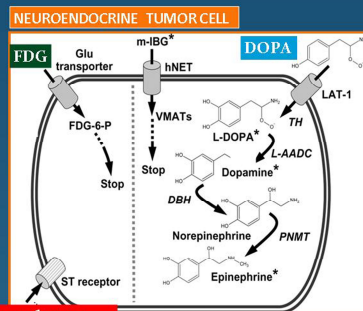


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INTRODUCTION

- > In patients with medullary thyroid carcinoma (MTC), rising levels of the tumour marker calcitonin after primary surgery indicate tumour recurrence or metastases
- > The only chance of cure is the resection of localised tumour tissue
- > Recently, various PET tracers have been proposed for the detection of recurrent disease in patients with MTC



Somatostatin analogues

Modified from Shulkin BL et al. Ann N Y Acad Sci 2006; 1073: 374-82

AIM

- > Aim of our study was to compare PET-CT with ⁶⁸Ga-somatostatin analogues, ¹⁸F-DOPA and ¹⁸F-FDG in a series of patients with suspected recurrent MTC on the basis of increased calcitonin levels during follow-up

METHODS

- > Among 40 patients previously operated for MTC (total thyroidectomy and loco-regional lymphadenectomy) who were submitted to ¹⁸F-DOPA PET-CT for increasing calcitonin levels, 18 patients (6 males and 12 females; mean age 53.5 ys.) who had performed also PET-CT with ⁶⁸Ga-somatostatin analogues (DOTANOC or DOTATOC) and ¹⁸F-FDG within 3 months were selected (Table 1).
- > PET-CT scans were classified as positive or negative on visual interpretation; number and site of abnormal foci detected by all methods were also recorded.
- > Comparison of the results of the three functional imaging modalities was done on a per-patient and on a per-lesion basis.
- > Verification of PET-CT findings was achieved by histopathology (in 13 cases) or imaging follow-up (in 5 cases).

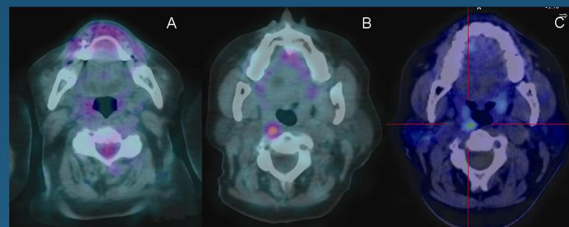
Table 2: Biochemical and imaging findings.

Patient	Time between surgery and PET imaging (months)	Calcitonin (pg/ml)	CTDT (months)	CEA (ng/ml)	Conventional imaging		¹⁸ F-DOPA PET-CT	¹⁸ F-FDG PET-CT	⁶⁸ Ga-somatostatin analogues PET-CT	Final diagnosis	Change in patient management	
					Type	Findings						
1	120	1840	6-12	280	US, MRI	Liver	Pos	Neg	Neg	Cyt	Yes	Im+ChE/RT
2	180	527	6-12	3.5	US, CT	Mediastinal LN	Pos	Neg	Neg	Cyt	No	FNAB
3	12	14186	< 6	160	US, CT, bone scan	Bone	Pos	Pos	Pos	Fup	No	STp
4	120	480	12-24	322	US, CT	Mediastinal LN, liver	Pos	Pos	Pos	Fup	No	W-S
5	96	12324	6-12	233	US, CT, bone scan	Bone	Pos	Pos	Pos	Fup	No	STp
6	192	992	< 6	9.9	US, CT	Neg/I	Pos	Neg	Pos	Hist	Yes	Im+biopsy
7	12	1573	> 24	13	US, CT	Neg/I	Neg	Neg	Neg	Fup	No	W-S
8	24	1829	> 24	40	US, CT, MRI	Neg/I	Neg	Neg	Neg	Fup	No	W-S
9	12	2043	12-24	24	US, CT	Neg/I	Pos	Neg	Pos	Cyt	Yes	FNAB
10	84	66.7	> 24	8	US	Neg/I	Pos	Neg	Neg	Cyt	Yes	FNAB
11	12	499	> 24	11.6	US, CT	Neg/I	Neg	Neg	Neg	Fup	No	W-S
12	36	300	> 24	7	US, CT	Neg/I	Neg	Neg	Neg	Fup	No	W-S
13	96	414	> 24	1.3	US, CT	Neg/I	Pos	Neg	Neg	Cyt	Yes	FNAB
14	156	1258	> 24	65.7	US, CT	Neg/I	Pos	Neg	Neg	Hist	Yes	Im+Surgery/RT
15	108	288	> 24	0.5	US, CT	Neg/I	Neg	Neg	Neg	Fup	No	W-S
16	36	226	6-12	20	US, CT	Neg/I	Pos	Neg	Neg	Fup	No	W-S
17	120	333	6-12	14.96	US, CT	Neg/I	Pos	Neg	Pos	Cyt	Yes	FNAB
18	36	132	> 24	3.1	US, CT	Neg/I	Pos	Neg	Neg	Cyt	Yes	FNAB

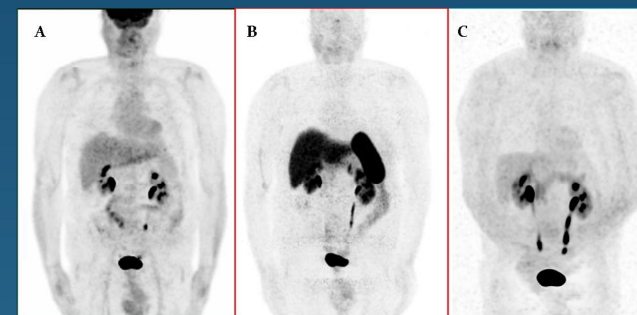
Legend: CTDT = calcitonin doubling time; Neg/I = negative or inconclusive; US = neck ultrasonography; LN = lymph node; Hist = histology; F-up = follow-up; Cyt = cytology; W-S = "wait and see"; FNAB = fine-needle aspiration biopsy; ChE = chemoembolization; RT = radiotherapy; STp = systemic therapy; Im = imaging.

RESULTS

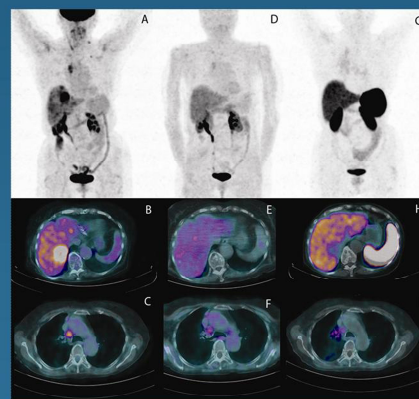
- > Main findings are described in Tables 2 and 3. Sensitivity of ¹⁸F-DOPA, ⁶⁸Ga-somatostatin analogues and ¹⁸F-FDG PET-CT was 72% (CI95%:50-88%), 33% (CI95%:16-56%) and 17% (CI95%:5-40%), respectively. In particular, 7 patients were positive at ¹⁸F-DOPA PET-CT alone. No patient was positive at ⁶⁸Ga-somatostatin analogues or ¹⁸F-FDG PET-CT alone.
- > Although increasing calcitonin levels, 5/18 (28%) patients were negative with all procedures.
- > In 10 cases ¹⁸F-DOPA PET-CT identified more lesions than ⁶⁸Ga-somatostatin analogues and ¹⁸F-FDG PET-CT, and in one case (with CEA=322ng/ml) ¹⁸F-FDG PET-CT revealed lesions missed by the other methods. No additional lesions were identified by ⁶⁸Ga-somatostatin analogues PET-CT.



A 62 year-old woman (patient n.9) with increased calcitonin and CEA levels after surgery for MTC underwent ¹⁸F-FDG, ¹⁸F-DOPA and ⁶⁸Ga-somatostatin analogues PET-CT. ¹⁸F-FDG PET-CT gave a negative result (A) whereas both ¹⁸F-DOPA (B) and ⁶⁸Ga-somatostatin analogues PET-CT (C) detected an area of increased radiopharmaceutical uptake in a right retropharyngeal lymph node. Fine needle agobiopsy confirmed the presence of MTC recurrence.



A 48 year-old man (patient n.11) with increased calcitonin and CEA levels after surgery for MTC underwent ¹⁸F-FDG (A), ¹⁸F-DOPA (B) and ⁶⁸Ga-somatostatin analogues PET-CT (C). All the three PET-CT modalities gave a negative result.



A 86 year-old woman (patient n.4) with increased calcitonin and CEA levels after surgery for MTC underwent ¹⁸F-FDG, ¹⁸F-DOPA and ⁶⁸Ga-somatostatin analogues PET-CT. ¹⁸F-FDG PET-CT showed multiple areas of abnormal radiopharmaceutical uptake in the liver and in cervical and mediastinal lymph nodes (A-C). ¹⁸F-DOPA PET-CT showed increased radiopharmaceutical uptake only in cervical and mediastinal lymph nodes (D-F), whereas ⁶⁸Ga-somatostatin analogues PET-CT showed only a weak radiopharmaceutical uptake in cervical and mediastinal lymph nodes (G-I).

CONCLUSION

- > ¹⁸F-DOPA PET-CT seems to be the most sensitive imaging method to detect recurrences in patients with MTC. Studies investigating larger patient population are needed to confirm these results and to explain the lack of abnormal uptake of all tracers in some cases.
- > In any case, the different uptake patterns observed with the various PET tracers reflect different metabolic pathways (uptake of hormone precursors, receptor expression, glucose metabolism); this information may help to broaden knowledge of MTC and potentially to select the most appropriate treatment.

Table 1: Patients characteristics.

Patient	Sex	Age	Inherited/sporadic MTC	Surgery	TNM
1	F	46	Inherited (MEN 2A)	TT+bCL	n.a.
2	F	25	Inherited (MEN 2B)	TT+bCL	n.a.
3	F	42	Sporadic	TT+bCL	pT3N1b
4	F	86	Sporadic	TT	T3N0
5	F	57	Sporadic	TT+bCL	pT3N1b
6	M	41	Sporadic	TT	pT1Nx
7	F	24	Sporadic	TT+bCL	pT1N1b
8	M	67	Sporadic	TT+rCL	pT1N1b
9	F	62	Sporadic	TT+rCL	pT3N1b
10	F	53	Sporadic	TT	pT1Nx
11	M	48	Sporadic	TT+bCL	n.a.
12	M	69	Sporadic	TT+bCL	pT4aN1a
13	M	59	Sporadic	TT+rCL	pT1N1b
14	F	77	Sporadic	TT	pT2N1b
15	F	51	Sporadic	TT+bCL	pT1N1b
16	M	49	Sporadic	TT	pT1Nx
17	F	40	Sporadic	TT	pT1Nx
18	F	61	Sporadic	TT	pT3Nx

Legend: TT = total thyroidectomy + central compartment lymphadenectomy; bCL = bilateral cervical lymphadenectomy; rCL = right cervical lymphadenectomy; n.a. = not available.

Table 3: PET-CT results on a patient- and a lesion-based analysis.

	¹⁸ F-DOPA PET-CT	¹⁸ F-FDG PET-CT	⁶⁸ Ga-somatostatin analogues PET-CT
Sensitivity on a patient based analysis (%)	13/18** (72)	3/18 (17)	6/18 (33)
Sensitivity on a lesion based analysis (%)	Local recurrence	1/1 (100)	0/1 (0)
	Lymph node	25/27** (98)	8/27 (30)
	Liver	23/32 (72)	9/32 (28)
	Bone	12/12 (100)	3/12 (25)
	Overall	61/72** (85)	20/72 (28)

Legend:
*: statistically significant difference vs ¹⁸F-FDG PET-CT;
*: statistically significant difference vs ⁶⁸Ga-somatostatin analogues PET-CT