stalks.[2,3] Calcified bodies are often seen in the stroma of papillomas.[3] An atypical papilloma is defined by the presence of mitoses >2 per 10 high power fields (HPF) and two or more of increased cellularity, nuclear pleomorphism, solid growth and areas of necrosis.[3]

There are only two other reports of choroid plexus papillomata arising in mature cystic teratomas in the literature. In one report a choroid plexus papilloma developed in the wall of an ovarian dermoid in a 14-year-old female.[4] In the other, an atypical choroid plexus papilloma with cytologic atypia, focal necrosis and mitoses up to 3/10 HPF, was described arising in the wall of a dermoid in a 26-year-old female.[5] Follow-up is limited in both cases.

Usual WHO grade I choroid plexus papillomata arising in the central nervous system are considered benign and complete excision in these cases is considered curative. By extrapolation, the oophrectomies performed to remove the teratoma in the current case and the other reported cases are considered curative.

Importantly, choroid plexus papillomata can be confused with other ovarian papillary epithelial neoplasms that may mimic primary or metastatic tumours including serous, clear cell or endometroid tumours, especially if associated with psammomatous calcifications.[6–8] Metastasis from lung adenocarcinoma, papillary thyroid carcinoma, urothelial carcinoma and malignant mesothelioma would also enter the differential diagnosis.[9]

In conclusion, we describe another example of the rare phenomenon of a choroid plexus papilloma arising in a mature cystic teratoma of the ovary. Pathologists need to be aware of this entity so as not to confuse this with other well differentiated ovarian papillary epithelial neoplasms that may be primary or metastatic.

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Metastatic papillary thyroid carcinoma to the kidney: report of two cases mimicking primary renal cell carcinoma and review of the literature

Sir,

Papillary carcinoma of the thyroid is the most common subtype, accounting for up to 86% of thyroid cancers. Mean age at diagnosis ranges from 31 to 49 years, with a female to male ratio between 2:1 and 3:1. The main pattern of spread is to cervical lymph nodes, with distant metastases occurring uncommonly and having an adverse impact on survival. Distant metastases from papillary carcinoma of the thyroid can occur at any time during the course of the disease: initial presentation of metastatic disease has been reported in 1–12% of differentiated thyroid tumours, being less frequent in papillary (~2%) than in follicular (~10%) thyroid carcinoma, whereas cumulative incidence, including metastatic disease following initial treatment, varies between 10 and 35%, depending upon the histology, again being least in well-differentiated papillary thyroid carcinoma.[1] Increasing age and primary size, male sex, extrathyroidal extension, and histological subtypes, including tall-cell, columnar-cell, diffuse sclerosing and solid variants, have been associated with adverse prognosis.[2] When haematogenous spread occurs, it is usually to bone, brain, lungs and soft tissue. Metastasis to the kidney is found in 2.8–3.8% and 6–20% of thyroid papillary and follicular cancer cases, respectively, but clinically detectable differentiated thyroid cancer metastatic to the kidney is exceedingly rare.[3]

Herein we report two cases of papillary thyroid carcinoma metastatic to the kidney. The literature on metastatic thyroid tumours to the kidney is also reviewed and differential diagnoses are discussed.

Case 1 was a 63-year-old man who presented in February 1995 with gastrointestinal symptoms, 10 lb weight loss and dizziness. He had a history of papillary thyroid carcinoma status post-thyroidectomy (1980), radical neck dissection and bilateral lung metastases (1982), iodine-131 treatment (1986), as well as chemotherapy (1991) and radiation therapy (1992). On admission, abdominal computed tomography (CT) scan showed a partially cystic mass in the right abdomen. The patient underwent angio-infarction and subsequent (5 months later) resection of a large right kidney mass eroding into the duodenum and forming a pyelo-duodenal fistula.

Grossly, most of the kidney was involved by a partially solid, cystic and extensively necrotic neoplastic process, 13 cm in largest dimension. Microscopically, the lesion showed a papillary architecture and characteristic nuclear changes (Fig. 1).

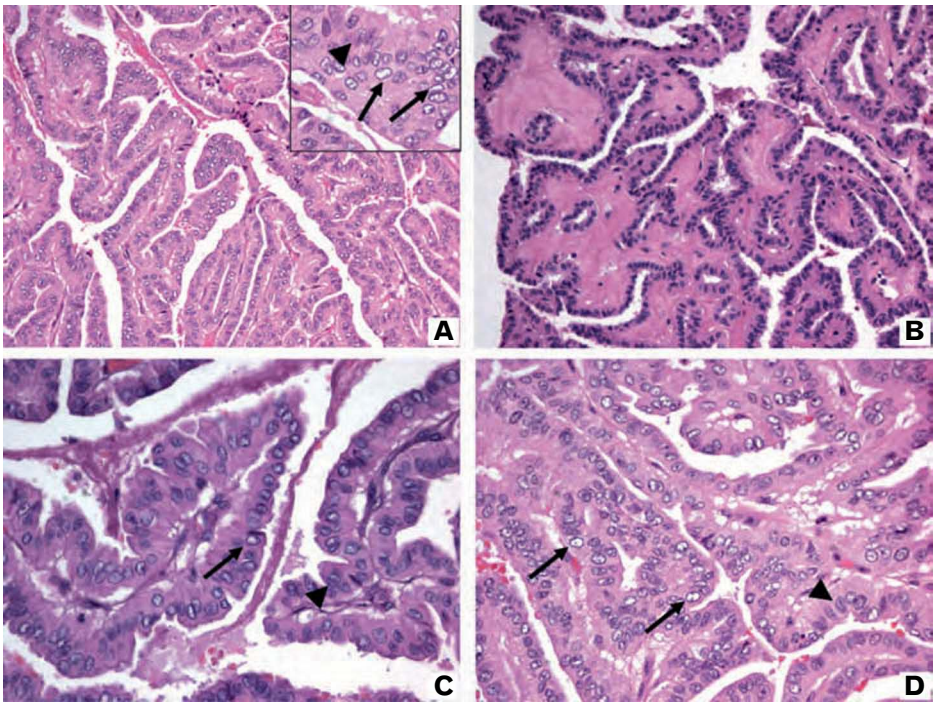

Fig. 1 Papillary carcinoma of the thyroid, tall-cell variant, metastatic to the kidney (H&E). (A) Neoplastic papillae are characterised by a central fibrovascular stalk of loose connective tissue and thin-walled vessels, and (B) in some cases show abundant acellular hyaline material. The papillae are lined by cells that often show abundant eosinophylic cytoplasm and are at least twice as tall as large. The nuclei (A, C, D) sometimes conform the elongated cells in which they are contained, and show the characteristic abnormalities of papillary thyroid carcinoma: optical clearing (arrows), indentations, folds and grooves (arrowhead).

Papillae showed a central fibrovascular stalk lined by neoplastic epithelium. The better developed papillae were long with a complex arborising pattern. Some were straight and slender, arranged in a parallel, regimented fashion; others were short and stubby. The papillary stalk was mainly composed by loose connective tissue and variously sized thin-walled vessels; in some cases, it was swollen by oedematous fluid or occupied by an abundant acellular hyaline material. Occasionally, it was infiltrated by lymphocytes or clusters of foamy or haemosiderin-laden macrophages. The neoplastic cells lining the papillae often showed tall cell features; they were at least twice as long (tall) as wide, with large eosinophilic cytoplasm and round to slightly oval nuclei. Nuclear contour appeared smooth on superficial examination, although closer inspection revealed subtle irregularities in the form of indentations, folds, and grooves. Another peculiar feature of neoplastic nuclei was the empty appearance of the nucleoplasm, which seemed almost totally devoid of chromatin strands. These nuclei were similar to the ones previously described as pale, optically clear, watery, empty, ground glass, or 'Orphan Annie's eyes'. No psammoma bodies or other concretions were noted. Immunohistochemically, neoplastic epithelial cells showed positive staining for cytokeratin (CK)19, CK7, CD57, thyroglobulin, and thyroid transcription factor-1 (TTF-1) (Fig. 2A–D). Cells did not react with CK20, racemase, HMWCK, p63, CD10, and RCC marker.

The histological and immunohistochemical findings supported the diagnosis of metastatic papillary thyroid carcinoma, tall-cell variant. The patient was lost to follow-up.

Case 2 was a 56-year-old woman who presented in December 2008 with haematuria and left flank pain due to an enlarging left lower pole renal mass. Her past medical history included metastatic papillary carcinoma of the thyroid, follicular variant to the brain (resected), thyroidectomy, resection of liver metastasis, and metastatic disease to the left arm treated by external beam radiation therapy. At ultrasound, a $7.9 \times 7.6 \times 6.0$ cm heterogeneous mass was identified at the inferior pole of the left kidney.

Needle biopsy of the renal mass showed variably-sized neoplastic follicles generally filled with homogeneous eosinophilic colloid. Follicles were lined by cuboidal epithelial cells with overlapping irregular nuclei that focally harboured characteristic changes of papillary thyroid carcinoma, such as grooves and intranuclear pseudoinclusions. No psammoma bodies or true papillations were identified. By immunoperoxidase staining, performed to further evaluate the lesion, the tumour cells showed positive reactivity for CK7, thyroglobulin, TTF-1, and CD57.

In view of the previous diagnoses the findings were considered consistent with metastatic papillary thyroid carcinoma, follicular variant. The patient underwent microsphere embolisation of the renal mass and died of disease, 7 years after her first diagnosis.

Metastatic disease to the kidney is observed frequently at autopsy, but is rarely found clinically in living patients.[3] Although there are no modern autopsy series devoted to kidney metastases, studies performed in the past have reported that renal metastases outnumber primary renal tumours by 4:1, and that up to 12.6% of cancer patients had metastatic disease to the kidney, with frequencies of bilaterality and multiplicity being as high as 71–81%. By contrast, primary renal cell carcinomas are rarely bilateral. Renal metastasis should be suspected whenever there is a known primary, even in cases of unilateral solitary renal masses. Although, theoretically, all solid tumours may give rise to renal metastasis, secondary lesions to the kidney occur more commonly in patients with lung and breast cancer, melanoma, gastric carcinoma and lymphoma. Reports in the literature suggest rates of epithelial (non-lymphoma) renal

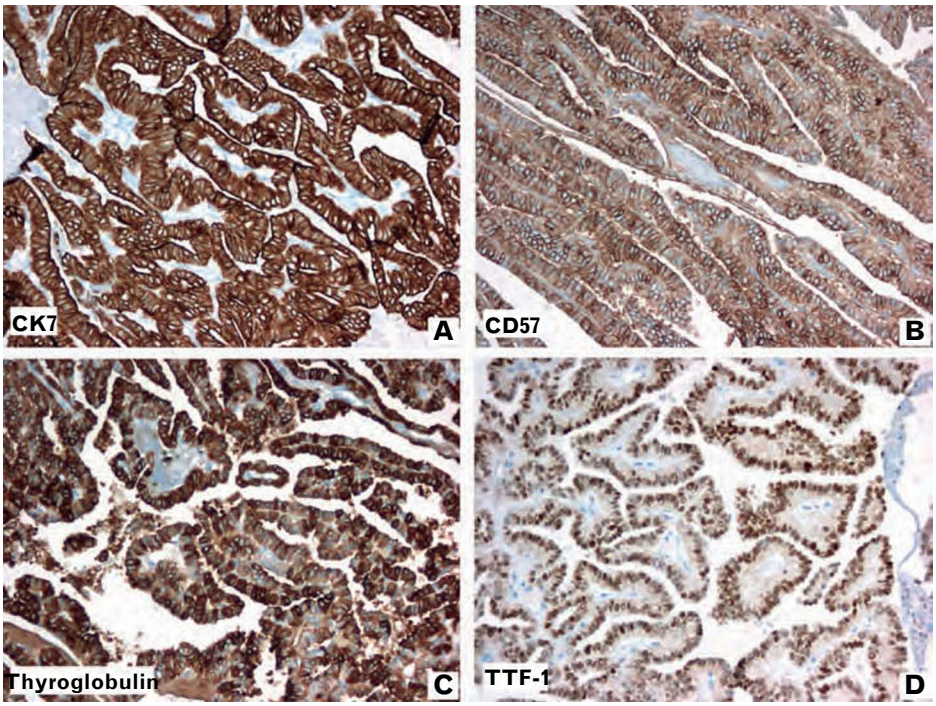

Fig. 2 Papillary carcinoma of the thyroid metastatic to the kidney (immunohistochemistry). Tumour cells show strong positivity for (A) CK7, (B) CD57, (C) thyroglobulin and (D) TTF-1.

metastases of 1.5–1.8% of the general population.[4] Imaging features are rarely pathognomonic.

Metastasis to the kidney of differentiated thyroid cancer is an uncommon event; in an autopsy series of 161 fatal primary malignant thyroid tumours, only four (6%) differentiated thyroid tumours metastasised to the kidney, whereas 35 (54%) and 40 (61%) metastasised to the lungs and bones, respectively.[5] In another autopsy study, Silliphant *et al*. found that six of 44 (14%) differentiated papillary and follicular thyroid cancers metastasised to kidney, compared to 22 (50%) and 17 (26%) cases metastasising to the lungs and bones, respectively.[6] On the other hand, thyroid cancer represents only 1.0–2.5% of primary tumours metastasising to the kidneys.[3]

Detection of thyroid carcinoma with clinically apparent kidney metastases is very rare, with less than 30 cases reported in the literature so far (21 of them referenced in Malhotra *et al*.).[7–12] Clinical and pathological features were only accessible in a subset of cases ($n = 28$) (Table 1). Of the 28 cases of renal metastases associated with differentiated thyroid carcinoma, 13 were from papillary carcinoma (7 of which were follicular-variant papillary carcinomas), and 15 were from follicular carcinoma. In five cases there was bilateral involvement. In three patients the disease was discovered incidentally during intravenous pyelography or ultrasound. In the vast majority of cases, patients had known thyroid tumours at the time the renal metastases were identified. However, in some instances, metastases to the kidney preceded the knowledge of the primary thyroid neoplasm and were treated surgically as primary renal tumours. Ruggiero *et al.* reported a case of a 25-year-old woman who underwent radical nephrectomy for a right renal mass.[7] The tumour was diagnosed as papillary thyroid carcinoma, follicular variant. The patient had no previous history of thyroid disease. During subsequent evaluation, metastatic disease was also identified in the patient's lungs. More recently, Gupta *et al*.[10] reported a case of metastatic papillary thyroid carcinoma that presented with flank pain and haematuria and was treated by radical nephrectomy as a primary renal malignancy. The patient had neither history nor signs and symptoms of thyroid disease. Later work-up of the patient for thyroid disease revealed a nodule of 0.6 cm in the right lobe of the thyroid, which was confirmed as a papillary thyroid carcinoma by ultrasound-guided fine needle aspiration. No other metastatic sites were identified.

Herein we describe two cases of thyroid papillary carcinoma, a tall-cell variant and a follicular variant, metastatic to the kidney. The former (Case 1) to our knowledge is the first case of tall-cell variant papillary thyroid carcinoma metastatic to the kidney described to date. Although both patients initially presented with disseminated disease, the renal metastasis presented as a unilateral, large heterogeneous mass located at the lower pole of the kidney.

The differential diagnoses for tall-cell variant papillary thyroid carcinoma metastatic to the kidney include primary papillary renal cell carcinoma, particularly type 2, micropapillary urothelial carcinoma of the upper urinary tract, and metastasis of papillary carcinomas from other organs. Papillary renal cell carcinoma comprises approximately 10% of renal cell carcinomas. The male to female ratio ranges between 1.8:1 and 3.8:1. Papillary renal cell carcinoma frequently contains areas of haemorrhage, necrosis and cystic degeneration. A pseudo-capsule may be identified. Bilateral and multifocal tumours are common. Neoplastic cells typically form varying proportions of papillae and tubules. Papillae contain a delicate fibrovascular core and aggregates of foamy macrophages; cholesterol crystals may be present. Calcified concretions are common in papillary cores and adjacent desmoplastic stroma. Papillary renal cell carcinoma has been subclassified into two morphological variants, types 1 and 2. Papillary renal cell carcinoma type 2 is composed of tall cell with eosinophilic cytoplasm and less frequently shows microcalcifications. Neoplastic cells exhibit large and spherical nuclei, prominent nucleoli, and varying degrees of nuclear pseudostratification,

Table 1 Clinical and pathological features of renal metastases from differentiated thyroid carcinoma

Reference	Sex/Age	Tumour type	Presentation	Years after detection	Site
Takayasu *et al.*, 1968[7]	F/44	Follicular	Abdominal mass	3	Bilateral
Davis *et al.,* 1979[7]	F/49	Follicular	Incidental finding (IVP)	18	Bilateral
Johnson *et al.*, 1982[7]	F/66	Follicular	Gross haematuria	37	Left kidney
Marino *et al.*, 1991[7]	F/–	Follicular	Neck nodule	23	Right kidney
Sardi *et al.,* 1992[12]	M/53	Papillary	Haematuria	7	Right kidney
Tur *et al.*, 1994[7]	F/72	PTC-FV	No complaints; liver mass	3	Right kidney
Ro *et al.*, 1995[7]	F/47	Follicular	Haematuria	7	Right kidney
Graham *et al.*, 1995[7]	M/75	PTC-FV	Gross haematuria	No previous history*	Left kidney
Lam *et al.*, 1996[11]	F/91	Follicular	Incidental autopsy finding	No previous history	Left kidney
Benchekroun *et al.*, 1999[7]	M/56	Papillary	Low back pain	3	Left kidney
Garcia-Sanchis *et al.*, 1999[7]	F/65	Follicular	Neck and sternal mass	No previous history	Left kidney
Gamboa-Dominguez *et al.*, 1999[9]	F/50	PTC-FV	Haematuria and flank pain	No previous history*	Left kidney
Muller *et al.*, 2000[7]	F/58	Follicular	Dyspnoea	11	Bilateral
Smallridge *et al*., 2001[7]	F/53	PTC-FV	Back pain	No previous history	Right kidney
Smallridge *et al.,* 2001[7]	F/61	PTC-FV	Upper back mass	No previous history	Left kidney
Abe *et al.*, 2002[7]	M/37	Papillary	Incidental finding (US)	No previous history*	Left kidney
Ferrer Garcia *et al.*, 2002[7]	F/58	Follicular	Lumbalgia	5	Left kidney
Moudouni *et al.,* 2002[7]	M/62	Follicular	Left upper abdominal discomfort	9	Left kidney
Insabato *et al*., 2003[7]	F/64	Follicular	Incidental finding (US)	35	Right kidney
Matei *et al.*, 2003[7]	F/78	Follicular	Microscopic haematuria and flank pain	10	Right kidney
Iwai *et al.*, 2005[7]	F/76	Follicular	Haematuria and flank pain	13	Right kidney
Liou *et al.*, 2005[7]	F/50	PTC-FV	Low back pain	No previous history	Right kidney
Ruggiero *et al.*, 2005[7]	F/25	PTC-FV	Abdominal/flank pain	No previous history*	Right kidney
Kumar *et al.*, 2005[7]	F/66	Follicular	Scalp mass	No previous history	Left kidney
von Falck *et al.*, 2007[7]	F/64	Follicular	Constant increase in serum thyroglobulin levels	20	Left kidney
Gupta *et al.*, 2008[10]	M/50	Papillary	Flank pain and haematuria	No previous history*	Right kidney
Malhotra *et al.*, 2010[7]	M/30	Papillary	Low backache radiating to the lower limbs	20	Bilateral
Borde *et al.*, 2011[8]	M/56	Papillary	Post radioiodine-131 treatment scanning	No previous history	Bilateral
Present cases:					
Case 1	M/63	Papillary	Nausea, vomiting, easy satiety	15	Right kidney
Case 2	F/56	PTC-FV	Haematuria and flank pain	6	Left kidney

* Treated surgically as primary renal cell tumour.
IVP, intravenous pyelogram; PTC-FV, papillary thyroid carcinoma - follicular variant; US, ultrasound.

although typical nuclear changes of papillary thyroid carcinoma are not present. Papillary renal cell carcinomas typically express CK7, CK8, CK18, CK19, CAM 5.2, RCC marker, CD10, and racemase (Table 2). Micropapillary urothelial carcinoma of the upper urinary tract is a rare variant of urothelial carcinoma. There is a male predominance (M:F = 3.2:1). Almost all the reported cases occur in the urinary bladder, but it may also involve the renal pelvis and the ureter. It consists of slender, delicate fine papillary and filiform processes, with central fibrovascular cores. Papillae are lined by high nuclear grade cells with eosinophilic cytoplasm. Psammoma bodies are infrequent. Micropapillary carcinomas are immunoreactive for CK7, EMA, CK20, Leu M1, and CEA.

The main differential diagnosis for the follicular variant of papillary thyroid carcinoma metastatic to the kidney is a recently described entity called 'primary thyroid-like follicular carcinoma of the kidney'. Other primary renal cell tumours, including oncocytoma, papillary renal cell carcinoma with tubular architecture, and metanephric adenoma should also be considered, although the presence of inspissated colloid-like material and/or follicular architecture is rare and patchy in these tumours.

Table 2 Immunohistochemical comparison between papillary thyroid carcinoma and papillary renal cell carcinoma

	PTC	PRCC
TTF-1	+	–
Thyroglobulin	+	–
CK17	+	–
CD57	+	–
Racemase	–/+	+
CD117	+	+/–
RCC marker	–	+
CD15	–/+	+
CK7	+	+
CK19	+	+
EMA	+	+

PRCC, papillary renal cell carcinoma; PTC, papillary thyroid carcinoma.

First reported in 2004, thyroid-like follicular carcinoma of the kidney is an extremely rare variant of renal cell carcinoma with only eight accepted cases described in the literature. This tumour shows a slight female predominance (M:F = 1:2). Histologically, these tumours are well circumscribed with a distinct fibrous capsule, a striking follicular architecture with micro- and macro-follicles filled with inspissated colloid-like material. The cells lining the follicles have moderate to scant amphophilic to eosinophilic cytoplasm. Nuclei are round to oval, with uniform chromatin and inconspicuous nucleoli. Although these tumours are usually incidentally detected, have a relatively small size, and a predominantly indolent behaviour, a distinct malignant potential is supported by reported metastatic disease in two patients. Thyroid-like follicular carcinomas of the kidney lack key histological features of papillary carcinoma of thyroid, such as papillary architecture and classic nuclear changes. Immunohistochemically, tumour cells are negative for classical markers of thyroid neoplasms such as thyroglobulin, TTF-1 and CD57. Pax2, RCC marker, CD10, WT1, Ksp-cadherin, racemase, vimentin, and CD56 have been reported to be negative. In a case recently diagnosed at the authors' institution, thyroid-like follicular carcinoma of the kidney showed strong nuclear staining for PAX8 (unpublished data, personal communication).

In conclusion, thyroid carcinoma should be considered in the differential diagnosis of a renal mass, particularly in patients with a high serum thyroglobulin level, even if the mass is solitary and unilateral, or no history of thyroid cancer is present. The overlapping profile between papillary renal cell carcinoma and metastatic papillary thyroid carcinoma highlights the importance of clinicopathological correlation, and demonstrates the importance of using a panel of antibodies in differentiating these tumours.

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Somatostatin receptor expression in prostate carcinoma: the urological pathologist's role in the era of personalised medicine

Sir,

Somatostatin (SST) is known to inhibit the secretion of a wide range of hormones, exocrine glands, and gastrointestinal motility. Among other actions, SST has revealed an antiproliferative potential, reversing the impact of mitogenic signals delivered by substances such as epidermal growth factor. The actions of SST are mediated by membrane-associated receptors that comprise five distinct subtypes (termed SSTR1 to 5). Frequently multiple subtypes coexist in the same cell.

After binding their ligand, SSTR-ligand complexes undergo cellular internalisation with intracytoplasmic and intranuclear translocation. Reubi *et al.*[1] showed that the degree of internalisation, i.e., the ratio of internalised SSTR2 to membranous SSTR2, varied greatly from one patient to the other. Although generally found in endosome-like structures, internalised SSTR2 were also identified to a small extent in lysosomes, as seen in colocalisation experiments. Very recently Waser *et al.*[2] showed that phosphorylated SSTR2 was present in most gastrointestinal neuroendocrine tumours from patients treated with octreotide but that a striking variability existed in the subcellular distribution of phosphorylated receptors among such tumours.

Cloning of the five SSTRs has led to the development of subtype-selective ligands.[3] In the era of personalised medicine and targeted therapies, SSTR profiling is an important prerequisite for successful *in vivo* somatostatin receptor targeting for imaging or therapeutic purposes in an individual patient. Therefore, localisation and expression of the five SSTRs in a tumour must be determined to decide whether the patient is eligible for these applications. Several methods have been used to determine the expression of SSRTs.

Tissue somatostatin receptors can be measured directly *in vivo* by performing a OctreoScan or 68 Ga-DOTATOC positron emission tomography/computed tomography scan. Molecular techniques such as *in situ* hybridisation histochemistry and autoradiography have been used in a limited number of studies.[4] The former basically investigates *SSTR* mRNA expression in cryostat sections. The latter also utilises cryostat sections and is based on radioligands, i.e., ^{125}I-labelled somatostatin ligands, such as octreotide. Previous studies have dealt with only some of the subtypes, therefore information is limited. The type of information obtained using these two techniques is not always comparable to that obtained with immunohistochemical analysis in formalin fixed, paraffin embedded (FFPE) tissue, in which the architecture and the cytology in the background are well preserved. In addition, the immunohistochemical technique is widely available, and faster, easier and cheaper to apply than *in situ* hybridisation histochemistry and autoradiography. It can be used even retrospectively on archival material.

We read with great interest the recent publication by Körner *et al.*[5] This study was performed on neuroendocrine tumours from various gastrointestinal and extragastrointestinal sites and in a small group of non-neuroendocrine tumours. The aim of the investigation was to correlate FFPE-based immunohistochemistry using the monoclonal anti-somatostatin receptor subtype 2A antibody UMB-1 (Biotrend Chemikalien, Germany; or Epitomics, USA), with the gold standard *in vitro* method quantifying somatostatin receptor levels in tumour tissues. The results obtained by comparing the UMB-1 immunohistochemistry with tumoural *in vitro* 125I-[Tyr3]-octreotide binding site levels allowed recommendations for the use of SSTR immunohistochemistry in daily diagnostics for optimally tailored patient management.

Data on the immunohistochemical patterns of the five SSTRs in prostate cancer (PCa), its precursor high-grade prostatic intraepithelial neoplasia (HGPIN) and normal prostatic