Case 11

Volumetric Perfusion CT for Early Assessment of Response to Anti-angiogenic Therapy in Metastatic Renal Cell Carcinoma

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History

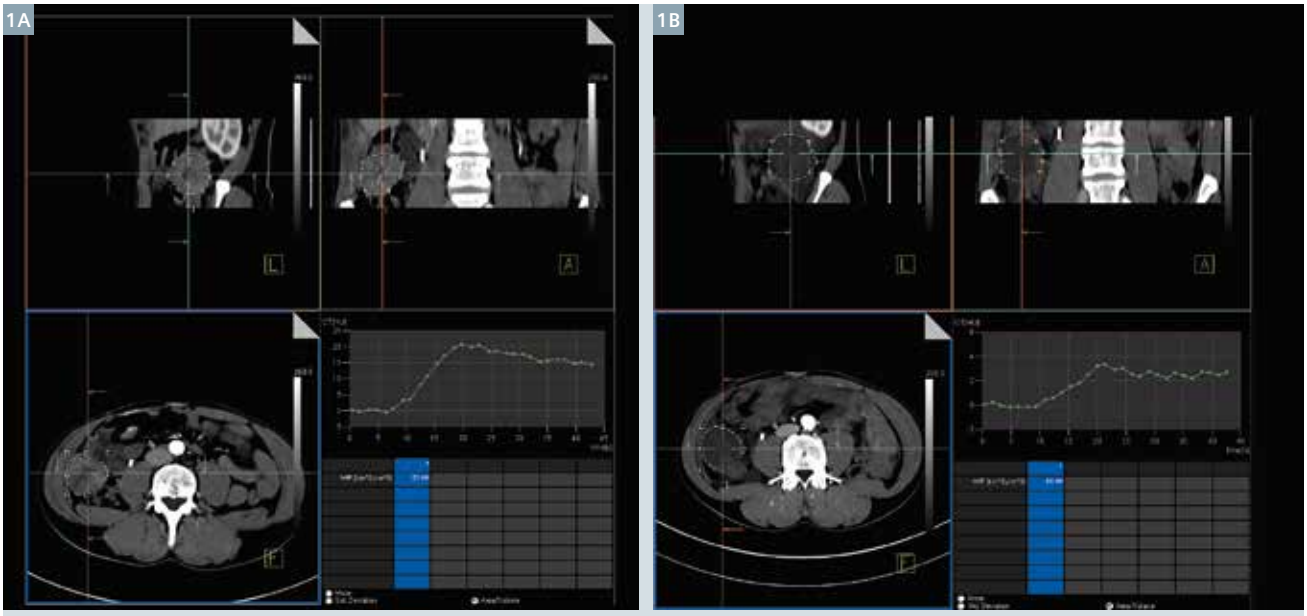
A 46-year-old male patient, with a right-sided partial nephrectomy due to papillary renal cell carcinoma one year ago, presented with tumor recurrence and new metastases in the right paracolic gutter and right abdominal wall. He was scheduled for anti-angiogenic tyrosin-kinase-inhibitor (TKI) therapy. Serial volumetric perfusion-CT scans of a selected representative metastatic lesion were performed, before as well as seven days after commencement of the anti-angiogenic TKI therapy, for noninvasive monitoring of early treatment response.

Diagnosis

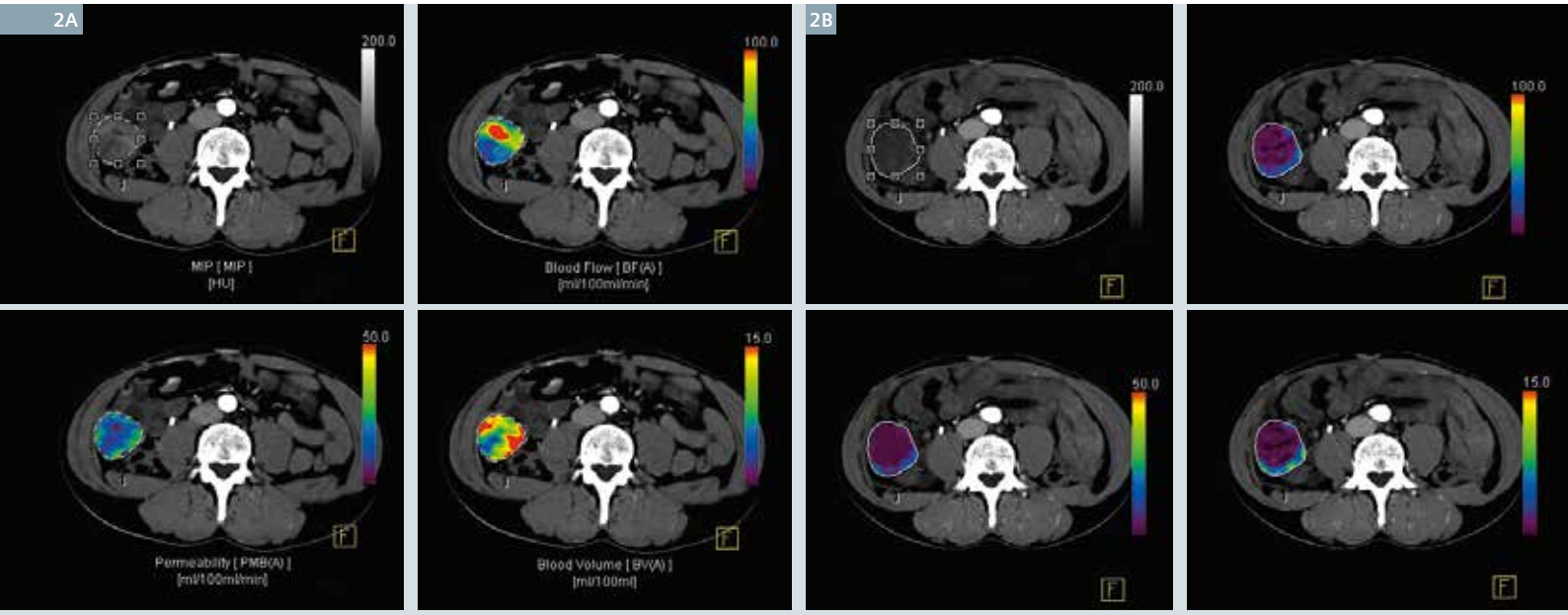
Volumetric perfusion CT analysis of the assessed target lesion, in the right paracolic gutter, (Fig. 1) showed increased baseline levels of tumor blood flow (BF), blood volume (BV) and vessel permeability (PMB) as features of tumor angiogenesis (Fig. 2A). A further perfusion CT scan performed after one week of TKI treatment which revealed a remarkable reduction in tumor perfusion indices (Fig. 2B) with a reduction in BF, BV and PMB levels of 70 – 80%, compared to their respective baseline values. On the other hand, tumor volume increased from about 53 mL (pre-treatment) to 89 mL (post-treatment) due to substantial tumor necrosis (Fig. 1). Based on the information from the perfusion CT scan, treatment was continued – despite the substantial increase in tumor size. Under ongoing TKI therapy, the patient is still in stable disease without further tumor growth (18 months after therapy begin).

Comments

With the introduction of anti-angiogenic therapy as a standard treatment in patients with metastatic renal cell carcinoma, new diagnostic challenges



1 Temporal MIP images of two serial perfusion CT scans centered around the metastatic target lesion in the right paracolic gutter, covering the entire tumor volume. After one week of TKI therapy, tumor volume increased from about 53 mL before therapy begin (Fig. 1A) to 89 mL post-treatment (Fig. 1B). However, as indicated by the time-resolved enhancement curves in the lower right quadrant of each figure, the contrast uptake within the tumor tissue had been reduced dramatically on day 7. Please note different scale of y axis in Figs. 1A and 1B.



2 Axial semi-quantitative color-coded VPCT parameter maps of the tumor perfusion indices (tumor blood flow, tumor blood volume and vessel permeability), acquired before treatment begin, depict regional heterogeneity of tumor vascularity with a mixture of hypervascular (colored in red) and hypovascular (colored in blue) areas (Fig. 2A). After 7 days of TKI therapy, the tumor has become almost completely hypovascular showing only small spots with residual perfusion (Fig. 2B).

arise in the assessment of therapeutic efficacy. Large clinical studies have shown that classical response criteria such as RECIST, which only take into account changes in tumor size, are of limited use in predicting long-term outcome in patients with metastatic renal cell carcinoma (mRCC).[1–3] This is – given the cytostatic rather than cytotoxic profile of anti-angiogenic agents – not unexpected. Functional imaging techniques, which quantitatively assess tumor perfusion such as perfusion CT, are currently being investigated as new biomarkers for predicting a response to anti-angiogenic therapy in cases of mRCC.[4] As changes in tumor vascularity precede morphological changes, perfusion CT may have the potential to aid physicians in evaluating therapeutic response in patients with mRCC at an early stage. This case nicely illustrates that perfusion CT can depict therapy-induced changes in tumor vascularity, as early as 7 days after commencing anti-angiogenic treatment. Whether CT-perfusion imaging can be a valuable adjunct to monitor response and aid physicians in predicting the outcome of anti-angiogenic therapy, must be evaluated in further studies.

Considering the broad dissemination profile of mRCC, with possible tumor manifestations to virtually all organs, the assessment of tumor perfusion in this tumor entity is challenging. With its integrated motion correction and semi-automated tumor segmentation algorithms – automatically excluding intra-tumoral vessels or bony structures from the analysis – VPCT software is a versatile tool for quantitative analysis of volumetric CT-perfusion data of patients with systemic tumor manifestations such as mRCC. ■

References

[1] Motzer, R.J., et al., Pazopanib versus sunitinib in metastatic renal-cell carcinoma. N Engl J Med. 369(8): p. 722-31.

[2] Motzer, R.J., et al., Sunitinib versus interferon alfa in metastatic renal-cell carcinoma. N Engl J Med, 2007. 356(2): p. 115-24.

[3] Sternberg, C.N., et al., Pazopanib in locally advanced or metastatic renal cell carcinoma: results of a randomized phase III trial. J Clin Oncol. 28(6): p. 1061-8.

[4] Braunagel, M., et al., The role of functional imaging in the era of targeted therapy of renal cell carcinoma. World J Urol. 32(1): p. 47-58.

Examination Protocol

Scanner	SOMATOM Definition Flash
Scan area	Mid abdomen
Scan length	100 mm
Scan direction	Adaptive 4D Spiral
Scan time	44 s
Tube voltage	100 kV
Tube current	120 mAs
Dose modulation	N/A
$CTDI_{vol}$	125.83 mGy
DLP	1483.6 mGy cm
Effective dose	22 mSv
Rotation time	0.28 s
Slice collimation	32 × 1.2 mm
Slice width	3 mm
Reconstruction increment	2 mm
Reconstruction kernel	B20F
Contrast	300 mg/mL
Volume	50 mL + 50 mL Saline
Flow rate	6 mL/s
Start delay	8 s