Spectral Dual-Layer Detector CT: A New Independent Prognostic Tool in Metastatic Renal Cell Carcinoma

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BACKGROUND

- Development of check point immunotherapy (CPI) and tyrosine kinase inhibitors (TKI) in the treatment of mRCC has not been accompanied by a corresponding development in imaging biomarkers.
- Spectral Dual-Layer Detector CT (DL-CT) can separate X-ray photons, enabling generation of conventional CT and DL-CT series.
- The DL-CT series can be used for the quantification of iodine concentration (IC, mg/ml), thereby providing information that goes beyond conventional CT.
- The prognostic ability of DL-CT in patients with metastatic renal cell carcinoma (mRCC) remains to be assessed.

METHODS

- Patients with mRCC were included in a prospective cohort study (ClinicalTrials identifier: NCT03616951), Figure 1 and were treated with TKI (N=72): pazopanib (N=29), carbozantinib (N=18), sunitinib (N=18), axitinib (N=7), or CPI (N=43): nivolumab/ipilimumab (N=30), nivolumab (N=13).
- All baseline scans were performed on 64-row dual-layer detector Philips Spectral IQON.

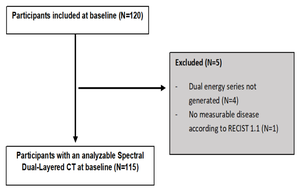

Figure 1. Flow chart

METHODS - cont

- A total of 115 participants and 313 target lesion were include at baseline, Figure 1 & Table 1.
- DL-CT scans were reconstructed to DL-CT and conventional CT series and used for quantification of iodine concentration (IC) and Hounsfield Units (HU) in the entire volume of all RECIST-defined target lesions using histogram analyses, and defined as IC(combined) and HU(combined), Figure 2.
- Data were analyzed as dichotomous variables (cut-off: median) and adjusted for treatments and IMDC risk factors and associated with PFS, OS and ORR (SPPS, v27)

Target Lesion Localization	% (n/N)
Kidney	8% (24/313)
Kidney bed	5% (16/313)
Lung / Pleura	28% (89/313)
Liver	10% (32/313)
Lymph nodes	25% (77/313)
Adrenal glands	7% (22/313)
Pancreas/Spleen	4% (13/313)
Bone (soft tissue component)	7% (21/313)
Muscle/soft tissue	4% (12/313)
Intra/retroperitoneal	2% (7/313)

Table 1. Target lesion localization

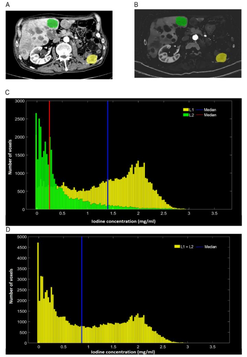

Figure 2 illustrates the method used for assessment of iodine concentration. Target lesion 1 (marked green) and target lesion 2 (marked yellow) were initially segmented on (A) the conventional CT series and (B) propagated to the iodine density series, where (C) a separate histogram for each target lesion was generated. Finally, the separate histograms were combined in to (D) one single combined histogram, where the median (blue line) was used for analyses.

RESULTS

- Patient baseline characteristics are illustrated in Table 2

Baseline characteristics	N (%)
IMDC risk group	
Favorable	19 (17%)
Intermediate	60 (52%)
Poor	36 (31%)
Male gender	86 (75%)
Prior nephrectomy	91 (79%)
Clear cell histology	100 (87%)
Age above > median (65.1 years)	57 (50%)
Line of Treatment	
1st line of treatment	77 (67%)
≥ 2nd line of treatment	38 (33%)
Treatment	
Tyrosine-kinase inhibitors	72 (63%)
Check point immunotherapy	43 (37%)

- The baseline median for IC(combined) and HU(combined) were:
  - IC(combined): 2.26 mg/ml (range,0.04-9.46)
  - HU(combined): 86.00 (range, 15.00-224.00).
- High IC(combined) was associated with longer PFS 24.2 vs. 8.4 months, *P*=0.003) and longer OS (35.8 vs 15.4 months, *P*<0.001), Figure 3.
- High HU (combined) was also associated with longer PFS (19.0 vs 8.7 months, *P*=0.02) and OS (35.8 vs. 16.3 months, *P*=0.001), Figure 3.

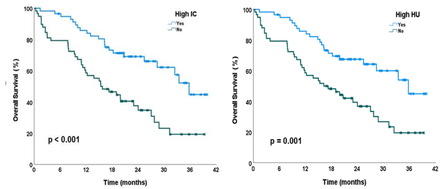

Figure 3 illustrates longer OS for patients with high baseline IC(combined) and HU(combined).

Multivariate associations with patient outcomes:

- High baseline IC(combined) was a favorable prognostic factors for the following outcomes, Table 3 and Figure 5:
  - -OS (HR=0.37, *P* <0.001) & PFS (HR=0.51, *P* =0.004)
  - -Treatment response (OR=4.35, *P*=0.001)
- High baseline HU(combined) was a favorable prognostic factor for the following outcomes, Table 4:
  - -OS (HR=0.42, *P* =0.001)
  - -Treatment response (OR=2.52, *P* =0.03)

Table 3. Multivariate association between baseline iodine concentration and outcome

	PFS		OS		ORR	
	HR (95% CI)	P	HR (95% CI)	P	OR (95% CI)	P
High IC(combined)	0.51 (0.32-0.80)	*0.004*	0.37 (0.22-0.63)	*<0.001*	4.35 (1.84-10.27)	*0.001*
Neutrophilia	2.10 (1.27-3.47)	*0.004*	2.28 (1.32-3.96)	*0.003*	-	-

Table 4. Multivariate association between baseline HU and outcome

	PFS		OS		ORR	
	HR (95% CI)	P	HR (95% CI)	P	OR (95% CI)	P
High HU(combined)	-	-	0.42 (0.24-0.72)	*0.001*	2.52 (1.12-5.69)	*0.03*
Neutrophilia	1.85 (1.11-3.08)	*0.02*	2.42 (1.39-4.23)	*0.002*	-	-
1st line of therapy	0.51 (0.32-0.81)	*0.004*	0.56 (0.34-0.94)	*0.03*	-	-
<1 year RCC to therapy	1.73 (1.03-2.90)	*0.04*	-	-	-	-

The C-index

- The C-index for IMDC risk factors was 0.650.
- The C-index increased to 0.687 when high HU(combined) was added.
- The C-index increased to 0.692 when high IC(combined) was added.

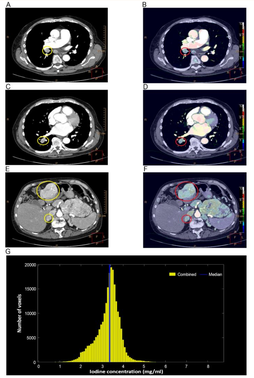

Figure 5 illustrates a patient with mRCC with four target lesions (A, C, E) on the conventional CT series (yellow circles) and (B, D, F) on the iodine overlay series (red circles), (G) with a high median iodine concentration (3.4 mg/ml) in the combined target lesions assessment. This participant had a long progression free survival (19 months) and is still alive (follow-up: 20+ months).

CONCLUSIONS

- IC(combined) and HU(combined) are new independent, prognostic imaging biomarkers in patients with mRCC, and may add to the prognostic accuracy of IMDC.

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