Mapping the Distribution of Brain Metastases in Renal Cell Carcinoma (RCC) and Association with Clinical Features

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Background

- Renal cell carcinoma (RCC) exhibits wide clinical and molecular heterogeneity with the capacity to metastasize to nearly any organ.
- Brain Metastases (BM) are frequently observed in metastatic RCC (mRCC) with a tendency to present with hemorrhagic BM and are associated with considerable morbidity and mortality.
- The incidence of BM in RCC according to previous reports is estimated to range from 5-15%.
- Most clinical trials in RCC, excluded patients who had a history of BM, thus, limiting prospective data on patients with RCC and BM.
- There is an unmet need to improve management strategies and outcomes in these patients.
- Recent emerging data from other solid tumors such as lung cancer showed that BM distribution patterns impact clinical outcomes and disease prognosis.
- However, distribution patterns of BM in RCC and associations with clinical outcomes are not well understood
- Here we present a detailed distribution analysis in a surgically resected BM RCC cohort with a focus on clinically relevant associations.

Methods

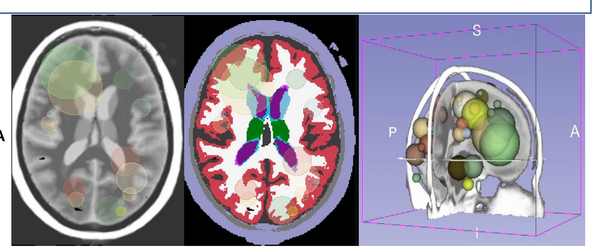
- Patients with metastatic RCC who underwent craniotomy for brain metastasis at JHU were retrospectively identified from our institutional database.
- Patients' demographics, clinical features, International Metastatic Database Consortium (IMDC) risk status, and treatment details were collected at the time of brain metastasis
- Survival outcomes assessed included CNS progression-free survival (PFS) and overall survival (OS) from the time of brain metastasis.
- We reviewed gadolinium-enhanced MRI brain and CT head (if available) at the time of BM diagnosis and assessed the presence of hemosiderin (susceptibility-weighted MRI) or hemorrhage (CT) in the BM.
- We marked each at their corresponding anatomic location in standard space as a sphere whose diameter was set to the largest measured diameter of the BM. Public brain atlases (Faria and Liu 10.25790/bml0cm.109; Vachet, SCR_002606) were used for distribution analysis. Serum prognostic markers were correlated with imaging (**Figure 1**).

Results

- Entire cohort included 46 patients with 67 BMs (**Table 1**)
- Posterior circulation and posterior cerebral artery territories contained 42% and 34% of BM despite supplying only 30% and 16% of the brain volume, respectively.
- 55% of the lesions were left-sided, 45% frontal, 21% parietal, 18% occipital, 7% temporal and 6% cerebellar.
- CNS progression-free survival was shorter in those who had renal vein thrombosis (7.3±1.7mo vs. 21.0±4.7mo, p=0.04), or had BM hemosiderin on imaging (16.8±3.8 vs. 37.7±21.5; p=0.04) (**Figure 2**)
- IMDC risk scores (log-rank p<0.001) predicted OS (**Figure 3**)
- On multivariable OS analysis, BM lateralized to the right (HR 2.6, p=0.06), hemosiderin in BM (HR 6.5, p=0.02) and IMDC risk groups (intermediate HR 2.9, poor risk HR 25.6, p<0.04) were independent prognostic factors for shorter OS (**Figure 4**)

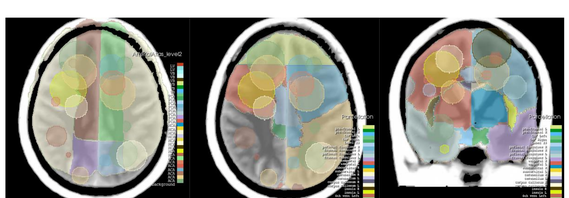
Figure 1A and 1B. Sample representation of brain metastasis mapping

1A



Standard space brain template (left) with anatomical structures highlighted (mid) and representation of lesions from this population in 3D (right)

1B



Examples of vascular distribution (left) and lobe (mid) maps from an axial and coronal (right) view

Table 1. Patients' characteristics

Patient Characteristic (n=46)	N, (%)
Number of BM lesions	67
Male Sex	35 (76%)
Age at BM diagnosis	63 (38-77)
RCC Histologic type	
Clear cell	42 (91%)
Non-clear cell	4 (9%)
KPS performance status	
> 80	38 (82%)
≤ 80	8 (18%)
IMDC at BM diagnosis	
Favorable	9 (20%)
Intermediate	28 (60%)
Poor	9 (20%)
Number of brain metastatic lesions	67
Mutilobar edema detected	24 (36%)
BM hemosiderin on MRI	80%
BM hemorrhage on CT	82%
Mean tumor diameters (cm)	2.0±1.1cm
BM distribution (left/right)	
Left	55%
Right	45%
BM anatomical territory distribution	
Frontal	45%
Parietal	21%
Occipital	18%
Temporal	7%
Cerebellar	6%
Systemic therapy post BM diagnosis	
I/O	10 (22%)
VEGF-TKI	14 (30%)
mTOR inhibitors	6 (13%)

Abbreviations: BM; brain metastasis, RCC: renal cell carcinoma, BMI; Body Mass Index. I/O, Immune-Oncology. VEGF-TKI; Vascular endothelial growth factor tyrosine kinase inhibitors. mTOR; mammalian target of rapamycin.

Figure 2. Kaplan-Meier estimate of PFS (A) PFS according to renal vein thrombosis and (B) BM hemosiderin on imaging

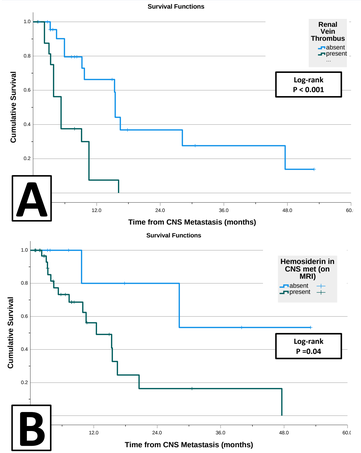


Fig 3. Kaplan-Meier estimate of OS in IMDC risk groups from the time of BM diagnosis

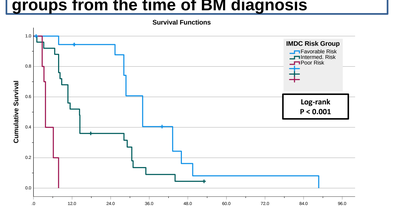
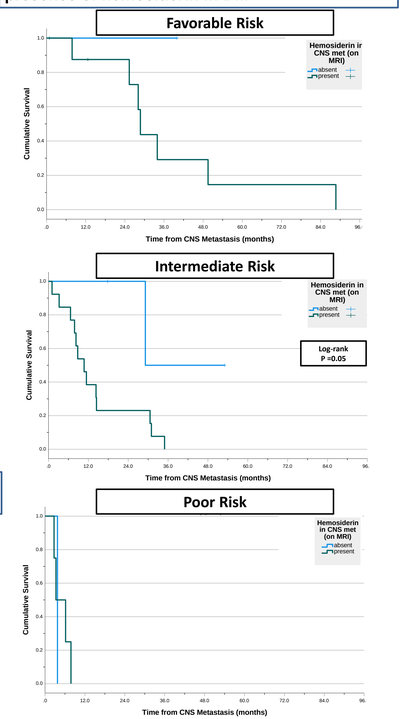


Figure 4. Kaplan-Meier estimate of OS from BM diagnosis in IMDC risk groups subdivided by the presence of hemosiderin in BM



Conclusions

- The above-presented lesion mapping method shows clinically relevant findings in RCC BM.
- Tumoral hemosiderin deposits appear a potential parameter to predict outcomes in RCC BM which deserve further study and validation.
- The study included surgically resected cohort, further analyses in a non-surgically resected cohort are underway.