MRI-characteristics of Pediatric- and Young Adolescent Renal Cell Carcinoma
a single-center retrospective study and literature review

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No disclosures

Introduction

- **Renal cell carcinoma (RCC)** → 2-6% of malignant pediatric renal tumors

- Rapidly rising incidences **second decade of life**

- **Pediatric RCC** → distinct entity
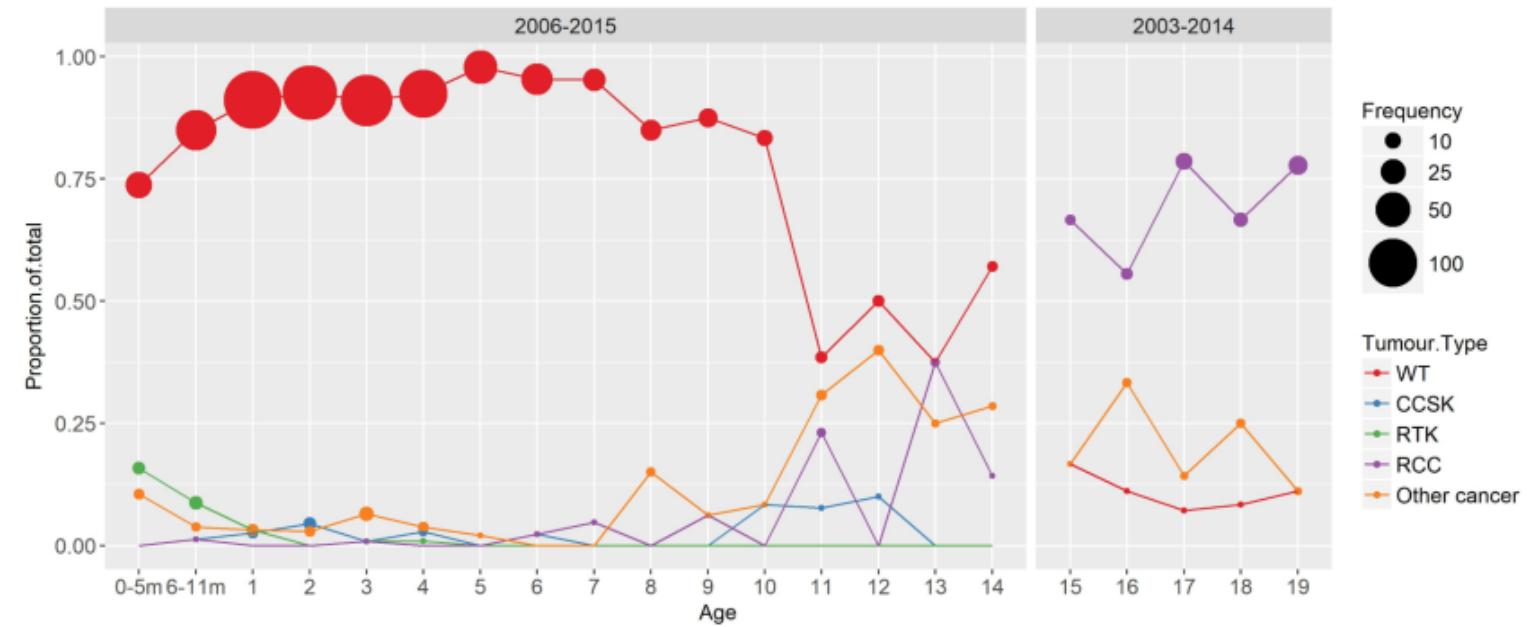
Histological subtypes

- **Histological subtypes** → predominantly translocation-type RCC (MiT-RCC)
  - MiT-family translocations *(TFE3, TFEB)*

- **Adults** → predominantly clear-cell type RCC
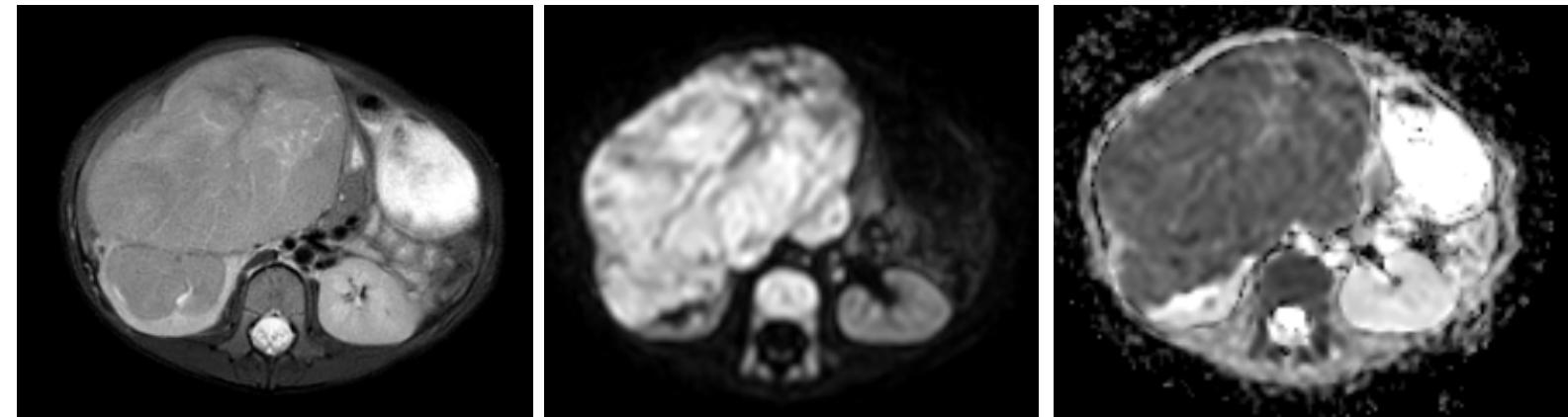
Clear-cell type RCC in 5-year old patient

Imaging

- **MRI (+ DWI)** → SIOP-RTSG 2016 UMBRELLA protocol

- **MRI-characteristics** of pediatric (and young-adolescent) RCC →
  - No pathognomonic characteristics
  - Limited studies
  - Differences adults ←→ children

- **Aim** →
  - Retrospective case series focused on diagnostic MRI-characteristics
  - Literature review MRI-characteristics RCC

Literature review

- **"MRI-characteristics of RCC"**
  - MiT-RCC
  - Children (and young-adolescents ≤35 years)
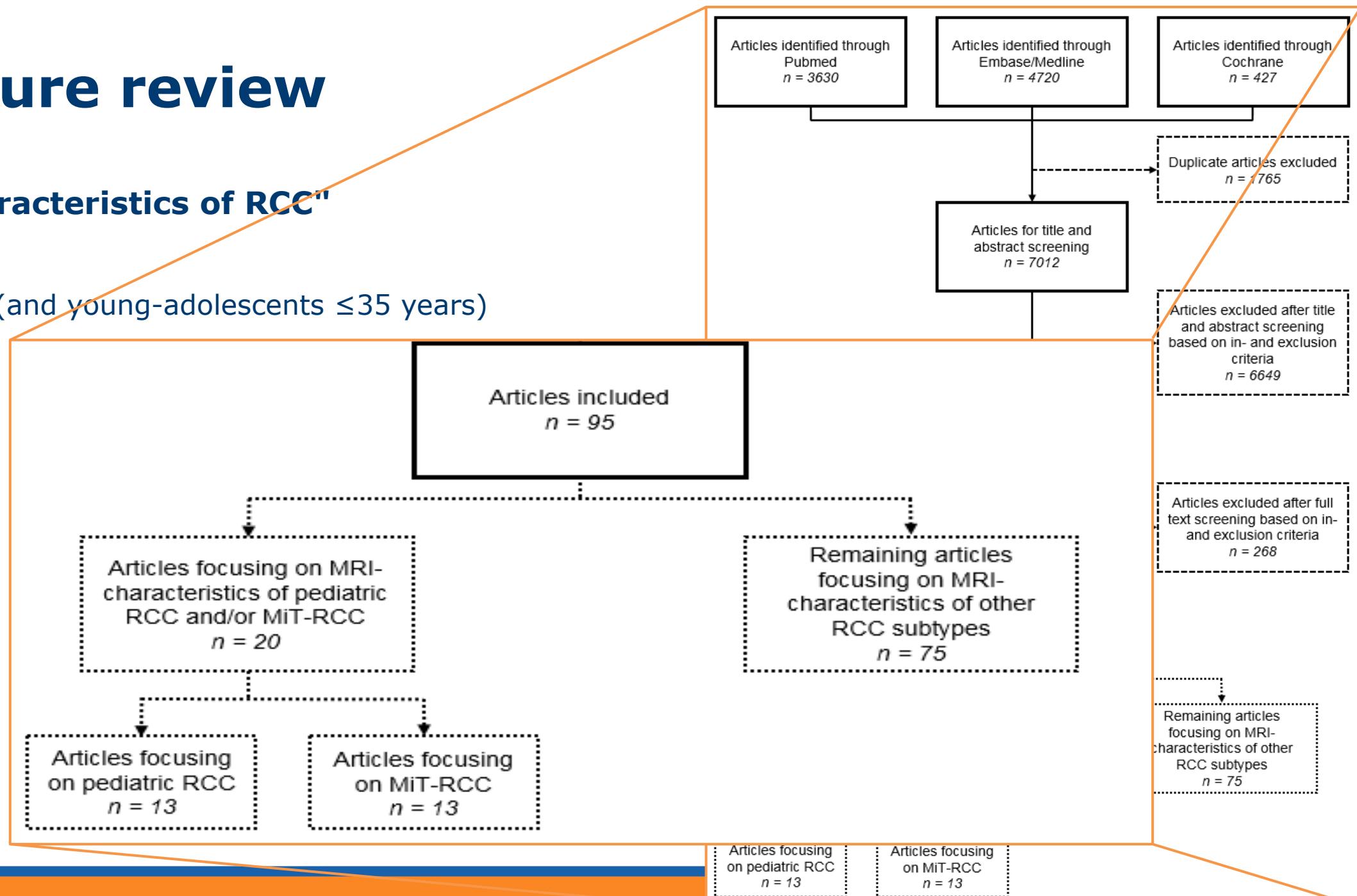
Literature review
MRI-characteristics of MiT-RCC

- **13** studies, **46** patients (**6** studies focusing on pediatric RCC)

- T1W **Hyper**-intensity ⟷ T2W **Hypo**-intensity

- **Heterogeneous** enhancement

- Cysts, Hemorrhage, Necrosis → often not specified

- **Infiltrative / Irregular** growth pattern

- **Limited diffusion restriction**

- *Smaller size*

> T2W hypo-intensity, Heterogeneous tumors, Relatively aggressive growth pattern

Tohi Y et al. *Int Cancer Conf J 2021* Dai C et al. *Abdom Radiol (NY) 2019* Gong P et al. *Medicine 2018* Chen X et al. *Eur Radiol 2017* Schaefer BA et al. *Pediatr Transplant 2017* Yu L et al. *Diagn pathol 2016* D'Antonio A et al. *Int J Surg Pathol 2016* Liu K et al. *JMRI 2014*
Wang W et al. *PLoS One 2014* Koo HJ et al. *Acta Radiol 2013* Dang TT et al. *J Comput Assist Tomogr 2012* Razek AA et al. *J Comput Assist Tomogr 2011* Kato H et al. *JMRI 2011* Jackson TJ et al. *Pediatr Blood Cancer 2022*

Case-series
Clinical characteristics

- **n = 6 patients** → median 12 years *(5-16 years)*

- Range tumor volume **29-2191 cm³**

- **2**/6 MiT-RCC – **2**/6 clear-cell RCC – **1**/6 FH-RCC – **1**/6 NOS RCC

Case-series
Solid tumor characteristics

- **Lobulated** tumors

- **Well-defined margins**

- Hemorrhage (**1**/6) – Necrosis (**1**/6) – Cysts (**2**/6)

- T1W **Iso**-intensity ←→ T2W **Hypo**-intensity

- **Homogeneous** enhancement

- No obvious correlation with histological subtype

**But, mainly interested in MiT-RCC.. →**
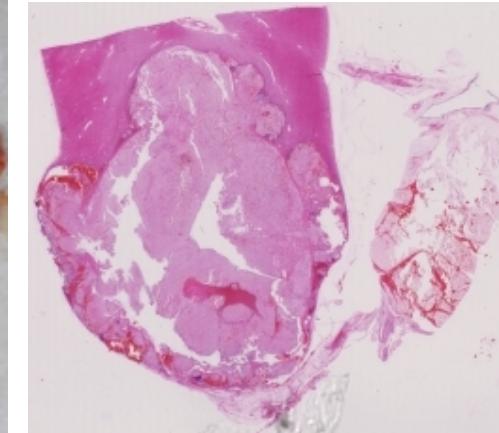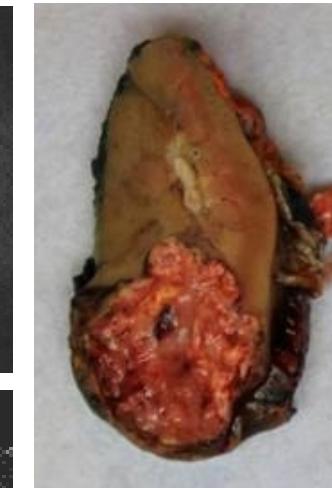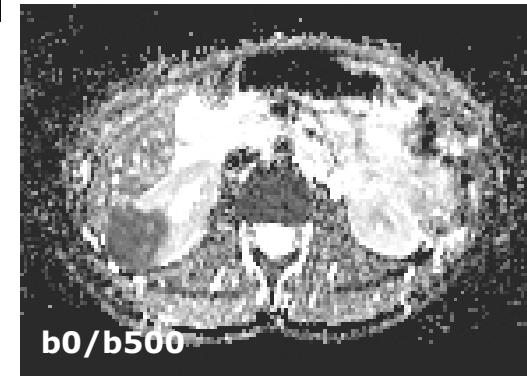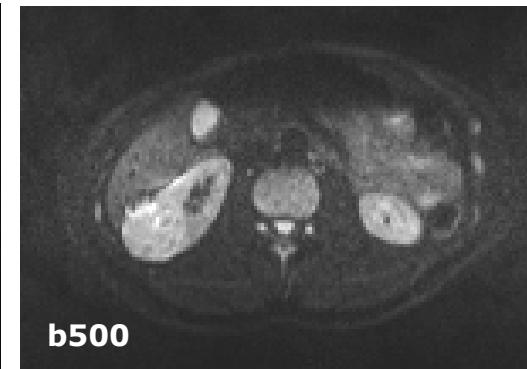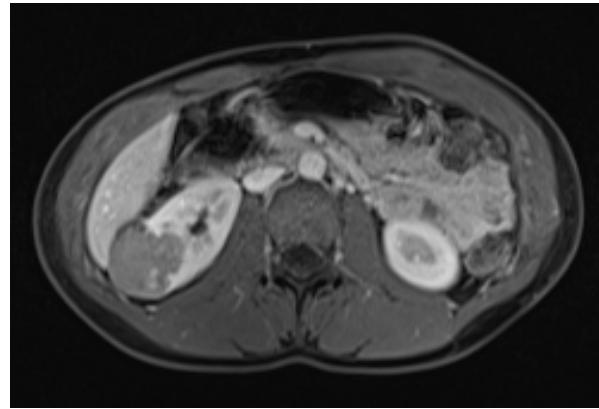
Case-series
MiT-RCC *(16-year-old male with left-sided MiT-RCC)*

b1000

b0/b1000
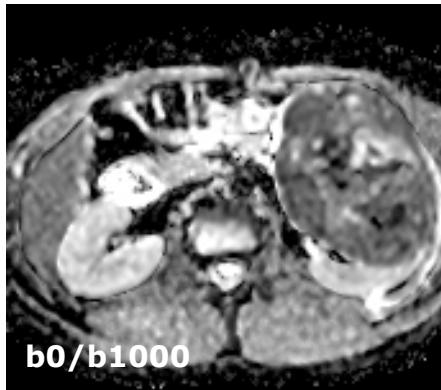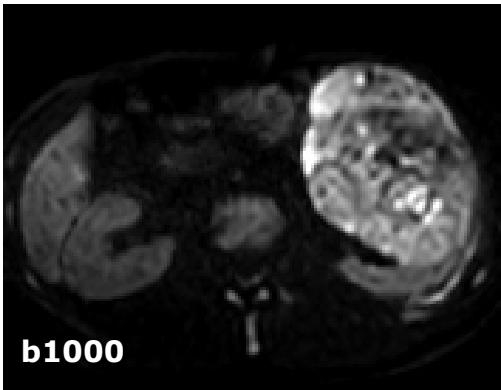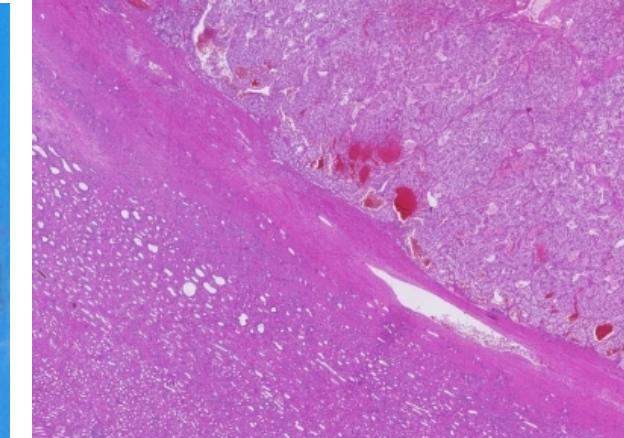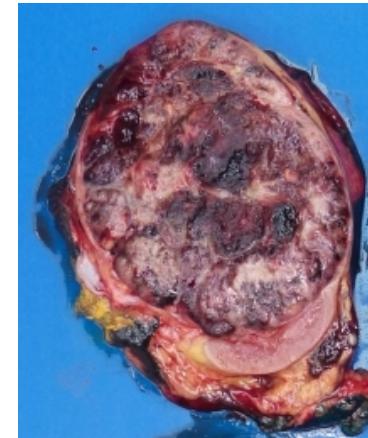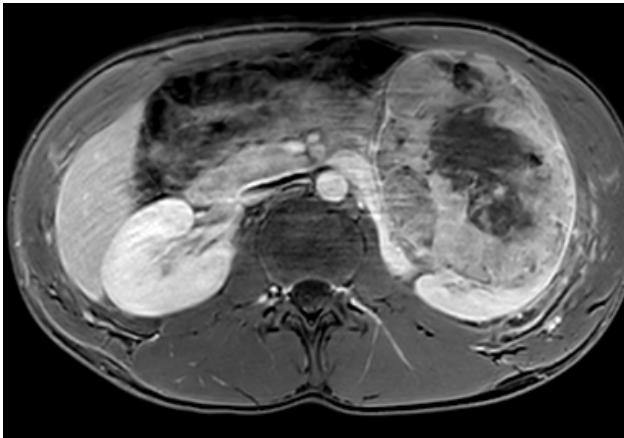
Conclusions

- **Varying presentation** in limited number of patients
- Specific MRI-characteristics pediatric RCC → remains **challenging**

- **T2-weighted hypo-intensity**

- Future aims →
  - **Discrimination** from other pediatric renal tumors
  - **Direct correlation** of MRI and histopathology

Acknowledgements

Collaborators

A.S. Littooij

M.M. van den Heuvel-Eibrink

R.R. de Krijger

R.A.J. Nievelstein

A. Bex
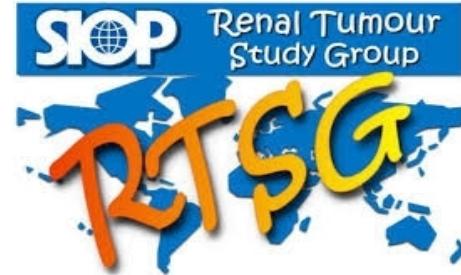
(Extra slices with tables in case of questions)

Literature review
MRI-characteristics of pediatric- and young-adolescent RCC

- **13** studies, **25** patients (age 4-33 years)

- **Heterogeneous** on T1W/T2W imaging and after iv contrast
- **Cysts, Hemorrhage and/or Necrosis** → often not specified
- **Regional lymph node involvement**
- **DWI** → limited information

Limited number of patients, **Variety of histological subtypes**, No consistency in characteristics

Noreña-Rengifo BD et al. *Cureus 2021*   Koetter P et al. *JPSCR 2020*   Schaefer BA et al. *Pediatr Transplant 2017*   Okabe K et al. *Int C Conf 2016*   Liu K et al. *JMRI 2014*   Wang W et al. *PLoS One 2014*   Koo HJ et al. *Acta Radiol 2013*   Dang TT et al. *J Comput Assist Tomogr 2012*
Downey RT et al. *Pediatr Radiol 2012*   Kato H et al. *JMRI 2011*   Blitman NM et al. AJR AMJR *2006*   Adachi T et al. *Int J Urol 2003*

Table 1. Scan parameters at 1.5-T MRI of the scanned sequences

Patient nr.	1	2	3	4	5	6
T2-weighted imaging						
Repetition time (ms)	7500	447	1400	454	2457	2457
Echo time (ms)	123	90	92	90	100	100
Slice thickness (mm)	5.5	1.15	4	1.15	5	5
Echo train length	17	85	256	85	39	39
Slicing gap	6.5	1.15	4.4	1.15	5	5
Acquisition matrix	320 x 224	348 x 348	384 x 194	348 x 348	452 x 78	452 x 78
T1-weighted imaging						
Repetition time (ms)	6.3	5.5	4.7	5.4	5.5	5.5
Echo time (ms)	3.1	2.7	2.4	2.7	2.7	2.7
Slice thickness (mm)	5	3	3	3	3	3
Echo train length	1	60	1	60	60	60
Slicing gap	2.5	1.5	NS	1.5	1.5	1.5
Acquisition matrix	288 x 192	232 x 233	320 x 170	232 x 233	232 x 233	260 x 261
Diffusion weighted imaging						
Repetition time (ms)	13333	2084	5300	2084	2398	2398
Echo time (ms)	634	72	75	72	73	73
Slice thickness (mm)	6	5	6	5	5	5
Echo train length	1	35	1	35	35	35
Slicing gap	7.2	5	7.2	5	5	5
Acquisition matrix	NS	88 x 70	192 x 153	88 x 70	88 x 70	88 x 70
b-values	0/50/600/1000	0/50/200/400/800	0/500	0/50/200/400/800	0/100/1000	0/100/1000

ms = milliseconds; mm = millimeters; NS = not specified

Table 2. Characteristics of the included pediatric patients with RCC

Patient nr.		1	2	3	4	5	6
Clinical characteristics	Age *(months)*	184	63	179	109	63	193
	Sex	Female	Female	Female	Male	Female	Male
	Tumor side	Right	Left	Right	Left	Right	Left
	Pre-operative chemotherapy	No	Yes	No	No	Yes	No
	Surgical approach	TN	TN	TN	TN	TN	TN
	Tumor stage	1	1	2	3	1	3
	Biopsy performed	No	No	Yes	No	No	No
Pathology findings	Weight of the specimen *(gram)*	2100	NS	210	610	753	820
	Tested for MiT-RCC *(test)*	No	Yes *(FISH)*	Yes *(FISH)*	Yes *(FISH)*	Yes *(FISH, RNA-seq)*	Yes *(RNA-seq)*
	Histopathological subtype	FH-RCC	ccRCC	MiT-RCC	NOS	ccRCC	MiT-RCC
	Genetic analysis	FH-mutation[d]	NS	NS	NS	None	NS
General tumor characteristics on MRI	Tumor volume *(cm³)*	2191	110	29	353	433	554
	Location of the tumor	Indist	Central	Peripheral	Peripheral	Central	Indist
	Regional lymph nodes	No	No	No	No	No	No
	Shape	Lobulated	Round	Lobulated	Lobulated	Lobulated	Round
	Margins	Well-def	Well-def	Ill-def	Ill-def	Well-def	Well-def
	Pseudocapsule	Yes	Yes	No	No	Yes	Yes
Growth pattern on MRI	Capsule rupture / invasion	No	No	Yes	Yes	No	No
	Infiltrative growth pattern	No	No	Yes	No	No	No
	Venous invasion / Tumor thrombus	No	No	No	No	No	No
MRI characteristics of solid components of the tumor	T2W imaging — Pattern	Hetero	Homo	Homo	Homo	Homo	Hetero
	T2W imaging — Intensity	Hypo, Iso	Iso	Hypo	Hypo	Hypo	Hypo
	T1W imaging — Pattern	Hetero	Homo	Homo	Homo	Homo	Hetero
	T1W imaging — Intensity	Iso	Iso	Iso	Hypo	Iso	Hypo
	Enhancement, degree and pattern	Strong, homo	Mild, homo	Strong, homo	Strong, homo	NA[a]	Mild, hetero
	Hemorrhage, degree	No	Yes, ext[b]	No	Yes, minimal	No	Yes, min[c]
	Necrosis	No	No	No	No	No	Yes
	Cysts	Yes	Yes[b]	No	No	No	Yes
	Septation	No	No	No	No	No	No
	Fatty tissue	No	No	No	No	No	No
	Subcapsular fluid	No	No	No	No	No	Yes[c]
	Increased vascularity	No	No	Yes	Yes	No	Yes
	Median surface ROIs *(cm²)*	4.29	0.45	2.66	9.06	18.14	2.61
	Median ADC-value[d] *(*10⁻³ mm²/s)*	1.20	1.05	0.98	1.20	0.70	0.80

TN = total nephrectomy; NS = not specified; FISH = fluorescence in situ hybridization; RNA-seq = RNA-sequencing; RCC = renal cell carcinoma; FH-RCC = fumarate-hydratase deficient RCC; ccRCC = clear cell type RCC; MiT-RCC = translocation-type RCC; NOS = not otherwise specified; Indist = indistinguishable; def = defined; Hetero = heterogeneous; Homo = homogeneous; ext = extensive; min = minimal.

[a] No contrast-enhanced diagnostic MRI-scan available; [b] Hemorrhage of/in the cystic lesion; [c] Subcapsular fluid suspected of hemorrhage; [d] Hereditary Leiomyomatosis and Renal Cell Cancer

Table 3. Review of literature focusing on MRI-characteristics of pediatric- and young adolescent renal cell carcinoma

Author (Year)	Country	Nr. of patients	Age (years)	Sex (M:F)	Histological subtype	Study design	Tumor side (L:R)	Tumor size (largest diameter in cm)	Tumor location	T1 weighted imaging appearance	T2 weighted imaging appearance	Contrast-enhanced imaging appearance	Tumor composition and growth pattern	Necrosis (n/ or total)	Hemorrhage (n/ or total)	Vascular involvement (n/ or total)	Intra-tumoral fat	Regional lymph node involvement / Lymph node metastases (n/ or total)	(Distant) metastases other than lymph nodes
Norena-Rengifo (2021)	Col	1	12	1:0	RMC	CR	1:0	NS	central	inter	hetero, hypo	hypovascular	solid, infiltrative	1	NS	absent	absent	renal hilum, para-aortic	absent
Koetter (2020)	USA	1	16	0:1	P1	CR	1:0	17.3	exophytic	NS	NS	hetero	cystic-solid	1	NS	absent	NS	peri-aortic, pericaval	absent
Schaefer (2017)	USA	1	14	1:0	MIT	CR	0:1	5.2	upper pole	homo	hetero	NS	solid	NS	NS	absent	NS	absent	absent
Okabe (2016)	Japan	1	4	1:0	CHR	CR	0:1	2.5	NS	hypo	hetero, hyper	NS	well-defined	1	NS	NS	NS	NS	NS
Zhou (2016)	China	1	17	1:0	CCA	CR	B	0.2-2.0[a]	B	hypo	hypo	strong	multiple B[a]	NS	NS	absent	NS	absent	synchronous CNS hemangioblastoma and pancreatic neuroendocrine tumor
Liu (2014)	China	3	15-33	1:2	MIT	CR	1:2	18; 6; 11	cortical	hyper	hetero, hypo	hetero hypo	solid (2); cystic (1); infiltrative (3)	focal (2), central (1)	Inter-tumor (3)	absent	NS	regional (2)	absent
Wang (2014)	USA	7[a]	13-33	3:4	MIT	RS	4:3	3.5-22	medullary (2); medullary cortical (4); exophytic (1)	iso (1); hyper (1); hetero (5)	hypo (1); hyper (1); hetero (5)	hetero: mild (1); moderate (4); marked rim/capsule (2)	irregular (6); not irregular (1) - well-defined (4); ill-defined (3)	7	6	3	NS	regional (4), cervical (1)	absent
Koo (2013)	South – Korea	1	28	0:1	MIT	RS	0:1	2.7	NS	NS	hetero, hyper	NS	well-defined	NS	NS	NS	absent	NS	absent
Dang (2012)	USA	2	18; 31	1:1	MIT	RS	0:1 B	8.9; 4.9	NS	hetero, hyper	NS	limited hetero (1); NS (1)	NS	1	2	absent	NS	absent	absent
Downey (2012)	USA	2[a]	NS	NS	NS	RS	NS	NS	NS	hetero, hyper (1); NS (1)	NS	hetero	NS	NS	intratumoral (1)	NS	NS	NS	NS
Kato (2011)	Japan	1	18	1:0	MIT	CR	0:1	4.1	peripheral	NS	hetero, hypo rim, central hyper	delayed peripheral hyper, rim hyper	well-demarcated	NS	NS	NS	absent (hemosiderin)	NS	NS
Bittman (2005)	USA	6 (3)[d]	15-27	3:3	RMC	RS	0:6	NS	central	NS	NS	hetero	infiltrative-ill-defined margins	4	intra-tumoral (4); sub-capsular (1)	ipsilateral renal vein (2); encasement vascular pedicle (3)	NS	cervical (6); retroperitoneal (5)[a]	liver (2); lung (3)
Adachi (2003)	Japan	1	4	1:0	CCP	CR	1:0	NS	NS	NS	NS	hyper walls	complicated cyst	NS	cystic (1)	NS	NS	absent	absent

[a] Multiple (cystic and) bilateral lesions in patient with von Hippel-Lindau disease; [b] MRI findings were not specified for each patient separately, so two adult patients (36 and 46 years old) could not be excluded from the overall MRI-data, but were not included in the clinical characteristics data; [c] Total of nine children but only 2 with MRI-scan and no specific details for separate patients (5:4 sex, mean age 12.9 years with a range of 7-17 years, mean maximum diameter 6.2cm (1.5-12.6)); [d] Imaging characteristics were not reported separately per patient, leaving no opportunity to extract MRI-specific information. Information displayed is for all 6 patients, based on CT and MRI; [a] Retroperitoneal adenopathy was heterogeneous and ranging in volume from small (n=1) or moderate (n=2) to extensive (n=2); Col = Colombia; RMC = renal medullary carcinoma; CHR = chromophobe RCC; CC = clear-cell RCC; P1 = papillary type 1 RCC; CCP = clear-cell papillary type RCC; CS = case report; RS = retrospective cohort study; B = bilateral; homo = homogeneous; hetero = heterogeneous; hypo = hypo-intense; iso = iso-intense; hyper = hyper-intense; inter = intermediate; incr = increase; CNS = central nervous system; NS = not specified.

Table 4. Review of literature focusing on MRI-characteristics of translocation-type renal cell carcinoma (MiT-RCC)

Author (Year)	Country	Nr. of patients	Age (median years, range)	Sex (M:F)	Study design	Tumor side (L:R)	Tumor size (largest diameter in cm)	Tumor location	T1 weighted imaging appearance	T2 weighted imaging appearance	Contrast-enhanced imaging appearance	Diffusion restriction (ADC-value x10⁻³ mm²/s)	Tumor composition and growth pattern	Necrosis (n/ of total)	Hemorrhage (n/ of total)	Vascular involvement (n/ of total)	Intra-tumoral fat	Regional lymph node involvement / Lymph node metastases (n/ of total)	(Distant) metastases other than lymph nodes
Tohi (2021)	Japan	1	78	1:0	CR	R	2.0	posterior	iso	hypo	NS	no restriction[a]	well circumscribed, no capsule	NS	NS	NS	absent	absent	absent
Dai (2019)	China	16	47.4 (20-76)	9:7	RS	9:7	1.7-14.6	endophytic epicenter (14)	hypo (2), iso (5), hyper (9)	hetero (14); hypo (13), iso (6), hyper (2)	hetero (7)	hyper on DWI (b0/500) ((16)	irregular (9), regular (7); complete capsule (11), incomplete capsule (5); solid (11), cystic (2), mixed (3)	NS	5	2	absent	3	retroperitoneal space & liver (1); lung (1)
Gong (2018)	China	2	50; 45	1:1	CR	1:1	10.6; 5.2	upper pole (1); lower pole (1)	iso (1), hypo (1)	hypo (2)	hetero (1)	NS	irregular (1)	1	NS	absent	NS	1	absent
Chen (2017)	China	2	46; 30	0:2	RS	0:2	7.8; NS	NS	hetero iso (2)	hetero (2); hyper (1), hypo (1)	hetero (2)	Relatively high signal on DWI (b0/800) (1)	oval (17), irregular (4); solid (4), cystic (1), mixed (16)[b]	NS	NS	v. renalis (1)	NS	1	liver (1)
Schaefer (2017)	USA	1	14	1:0	CR	0:1	5.2	upper pole	homo	hetero	NS	NS	solid	NS	NS	absent	NS	absent	absent
Yu (2016)	China	1	40	1:0	CR	0:1	12	NS	iso	hetero hypo-hyper	NS	NS	well-defined, irregular	1	patchy (1)	absent	NS	1	absent
D'Antonio (2016)	Italy	1	71	0:1	CR	B[c]	12.0	NS	NS	hetero	hyper	NS	NS	poorly circumscribed (1)	1	1	NS	NS	NS	NS
Liu (2014)	China	4	15-45	1:3	RS	1:3	4-18	cortical (4)	hyper (4)	hypo (3), hyper (1)	Hypo	NS	infiltrative (4); solid (3), cystic (1)	focal (3), center (1)	inter-tumor (4)	absent	absent	lymphadenopathy (3)	absent
Wang (2014)	USA	9	13-46	3:6	RS	4:5	2-22	medullary (3), medullary cortical (4), exophytic (1), pelvis (1)	iso (1), hyper (3), hetero (5)	hypo (1), hyper (2), hetero (6)	hetero: mild (1), moderate (6), marked rim/capsule (2)	NS	capsule (3); irregular (8), oval (1); well-defined (5), ill-defined (4)	8	7	4	NS	regional (5), cervical (1)	absent
Koo (2013)	South Korea	2	28; 71	0:2	RS	0:2	2.7; 4.6	NS	NS	hetero, hypo (2)	NS	NS	well-defined (2)	NS	intra-tumoral (1)	NS	absent	NS	absent
Dang (2012)	USA	2	18; 31		RS	0:1 B	8.9; 4.9	NS	hetero, hyper	NS	limited hetero (1); NS (1)	NS	NS	1	2	absent	NS	absent	absent
Razek (2011)	Egypt	4	5-67[d]	NS	PS	NS	NS	NS	NS	NS	NS	mean 1.50 ±0.97 (1.37-1.62) (b0/800)	NS	NS	NS	NS	NS	NS	NS
Kato (2011)	Japan	1	18	1:0	CR	0:1	4.1	peripheral	NS	hetero, hypo rim, central hyper	delayed peripheral hyper, rim hyper	NS	well-demarcated	NS	NS	NS	absent (hemosiderin)	NS	NS

[a] Tumor showed no restricted diffusion with a low signal; a fat-poor angiomyolipoma was in the differential diagnosis; [b] Total study existed of 21 patients, of which only for 2 patients MRI-characteristics were reported. The tumor composition, shape and growth pattern are therefore reported for the total population, mainly based on CT; [c] Bilateral tumor, with a right conventional RCC, and a left MiT-RCC. Therefore the characteristics of the MiT-RCC are presented in the table; [d] Study with 55 patients, of which 4 had an MiT-RCC. Age, was presented for all patients.