Normal values in MAG3 scintigraphy

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Original Article

Thieme

Reference values for quantitative parameters in renal scintigraphy with Tc-99m-MAG3

Referenzwerte für quantitative Parameter in der Nierenszintigraphie mit Tc-99m-MAG3

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MAG3: history

Synthesis and Biological Evaluation of Technetium-99m MAG_3 as a Hippuran Replacement

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A new technetium-chelating agent based on a triamide monomercaptide tetradentate set of donor groups, mercaptoacetylglycylglycylglycine (MAG_3), was synthesized and evaluated. Chelation with ^{99m}Tc resulted in a single radiochemical product as expected. Studies in mice of [^{99m}Tc]MAG_3 indicated excretion rates faster than *o*-iodohippurate (OIH) both in normal and in probenecid treated animals. Specificity for renal excretion was essentially complete. Clearance studies in rats resulted in 2.84 ml/min/100 g for [^{99m}Tc]MAG_3, 2.17 for OIH, and 1.29 for [^{125}I]iothalamate. Extraction efficiencies were 85% for [^{99m}Tc]MAG_3, 69% for OIH and 39% for [^{125}I]iothalamate. Probenicid depressed the clearance both of [^{99m}Tc]MAG_3 and OIH at 25 and 50 mg/kg/hr, but to a greater extent with [^{99m}Tc]MAG_3. The greater effect is offset, however, by the larger fraction secreted by the renal tubular cells. The animal results suggest that [^{99m}Tc]MAG_3 may be a useful alternative to [^{131}I]OIH.

J Nucl Med 27:111–116, 1986

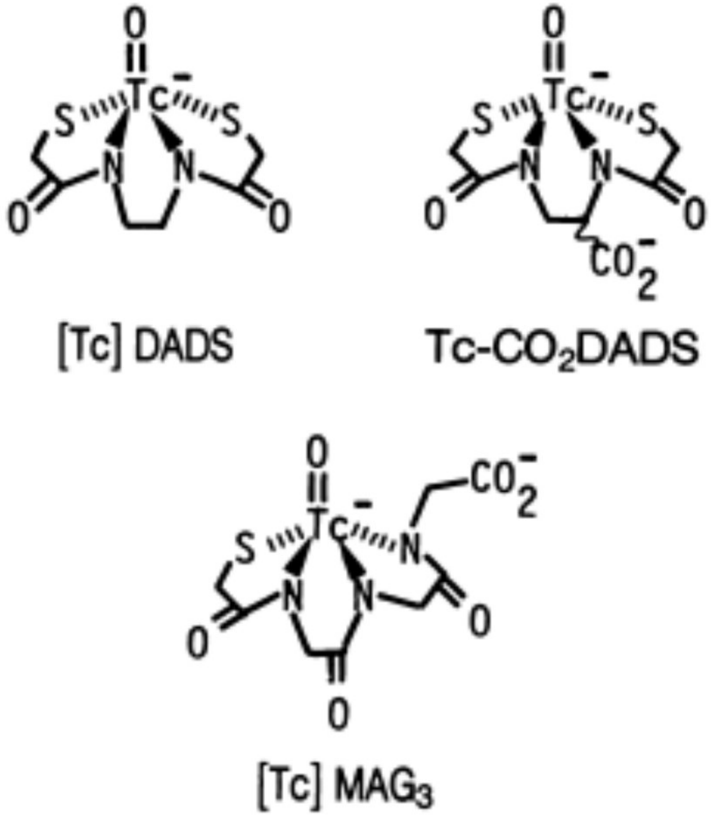

FIGURE 1
Structures of Tc-N_2S_2 (DADS) complexes and proposed structure of [Tc]MAG_3

MAG3: history

Comparison of Iodine-131 OIH and Technetium-99m MAG_3 Renal Imaging in Volunteers

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Department of Nuclear Medicine, University of Utah School of Medicine; and Veterans Administration Medical Center Salt Lake City, Utah

Animal studies have suggested that the nonisomeric N_3S triamide mercaptide ligand, ^{99m}Tc mercaptoacetyltriglycine (MAG_3), may provide a satisfactory ^{99m}Tc-labeled replacement for ^{131}I hippurate (OIH). Sequential 30-min [^{99m}Tc]MAG_3 (5-10 mCi) and [^{131}I]OIH (300 μCi) imaging studies were performed in ten normal volunteers in order to compare the image quality, renal excretion, blood clearance, and time to peak height of the renogram curve. In addition, [^{99m}Tc]MAG_3 (5 mCi) and [^{131}I]OIH (150 μCi) were administered simultaneously in eight volunteers for comparison of 180-min blood and plasma clearances and urine excretion. In the sequential imaging studies, the blood clearance of [^{99m}Tc]MAG_3 was more rapid than [^{131}I]OIH with a mean clearance of 1.30 l/min compared with 0.88 l/min for [^{131}I]OIH ($p < 0.05$). Seventy-three percent of the injected dose of the MAG_3 was excreted by 30 min compared with 66.8% for [^{131}I]OIH. Whole kidney and cortical renogram curves showed no significant difference in the time to peak height for MAG_3 and [^{131}I]OIH. In all subjects, the quality of the [^{99m}Tc]MAG_3 images were clearly superior to [^{131}I]OIH. Following simultaneous injection, blood and plasma clearances for [^{131}I]OIH were more rapid than MAG_3 when determined for multiple time intervals from 0–30 to 0–180 min ($p \leq 0.05$). The 0–30-min clearances of MAG_3 and [^{131}I]OIH were only slightly greater than the 0–180-min clearances and can be used to obtain valid comparisons of the two agents. As in the sequential study, 30-min urine excretion was greater for MAG_3 than [^{131}I]OIH (73.1 compared with 69.6%) but the difference was not statistically significant. Although the differences in the MAG_3 clearances following sequential and simultaneous administration are not satisfactorily explained, the fact that both clearances were rapid, the MAG_3 and OIH renogram curves were quite similar, and 30-min urine excretions of MAG_3 and OIH were essentially identical suggests that MAG_3 may become a ^{99m}Tc replacement for [^{131}I]OIH and further clinical evaluation is warranted.

J Nucl Med 27:795–803, 1986

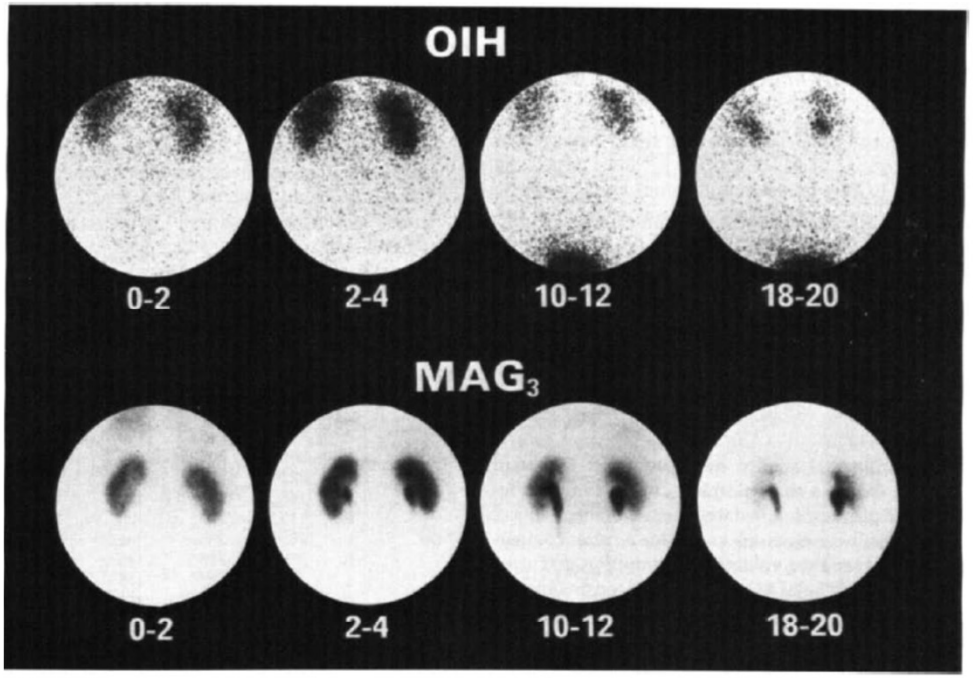
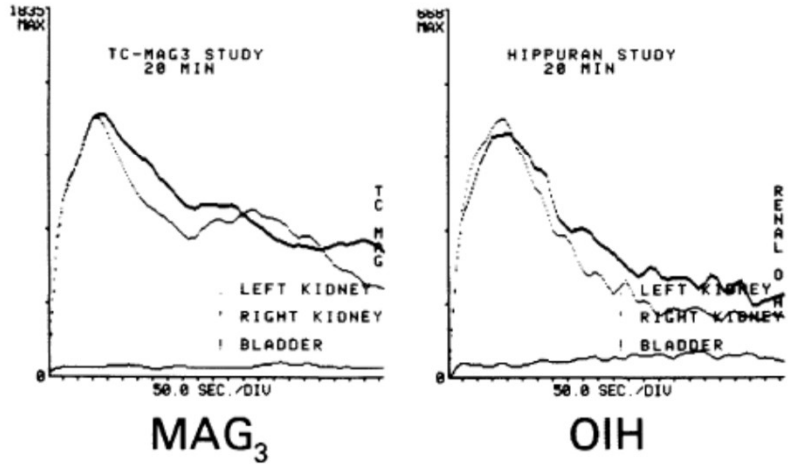


FIGURE 2
OIH and [^{99m}Tc]MAG_3 images for Subject 6 are shown at corresponding time intervals for comparison

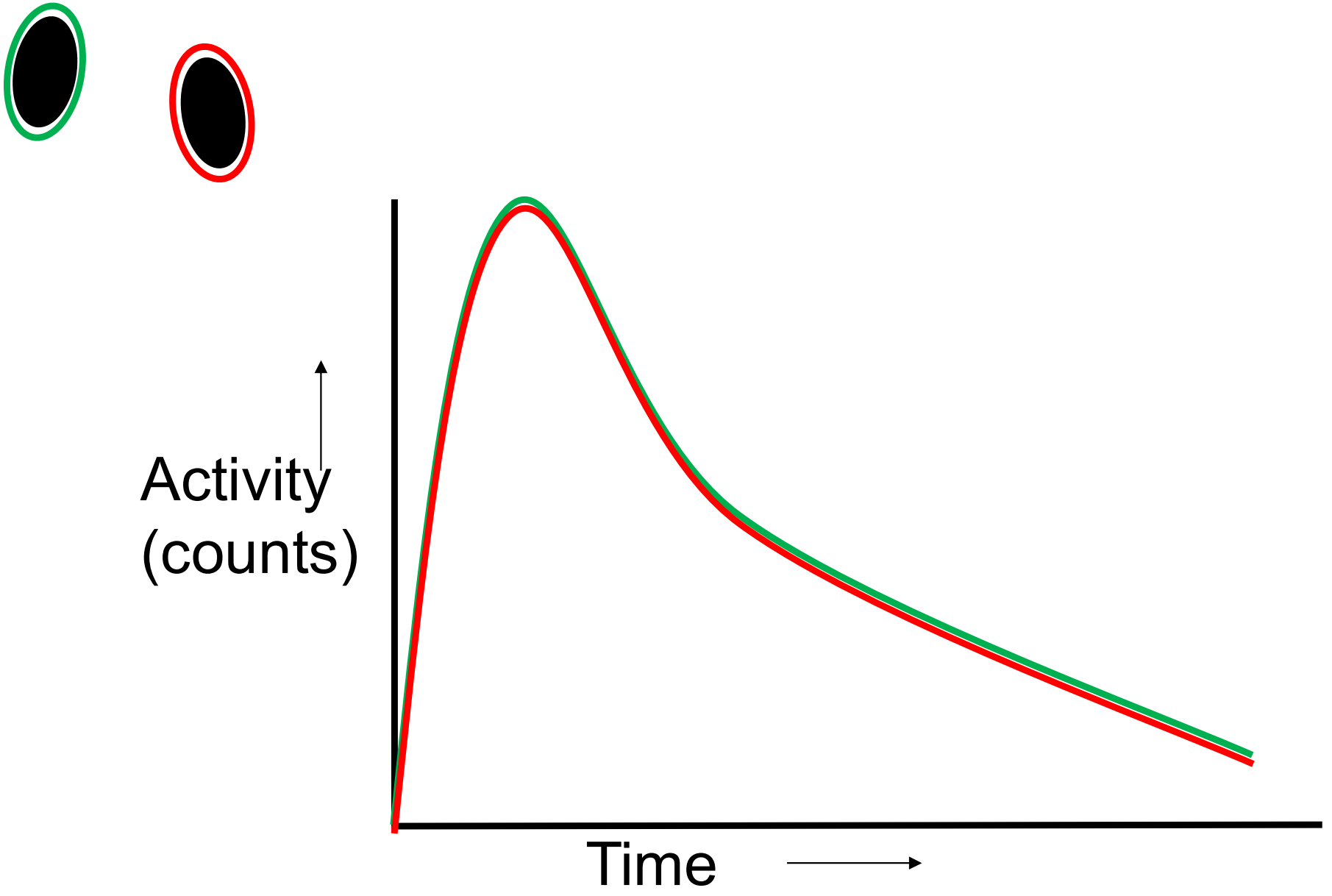


MAG3: clinical practice

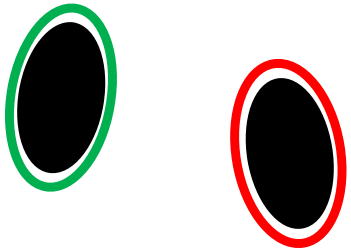
- Many different protocols used in clinical practice

- Variations in:
  - Activity given
  - Furosemide challenge (e.g. at all? Before MAG3? 15-20-30 minutes after MAG3?)
  - Post-miction acquisition or not

MAG3: Basic – ideal world



MAG3: Basic – Varieties



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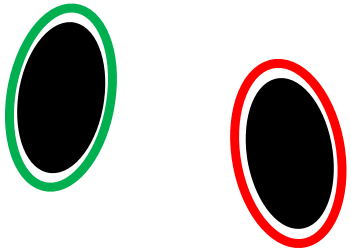

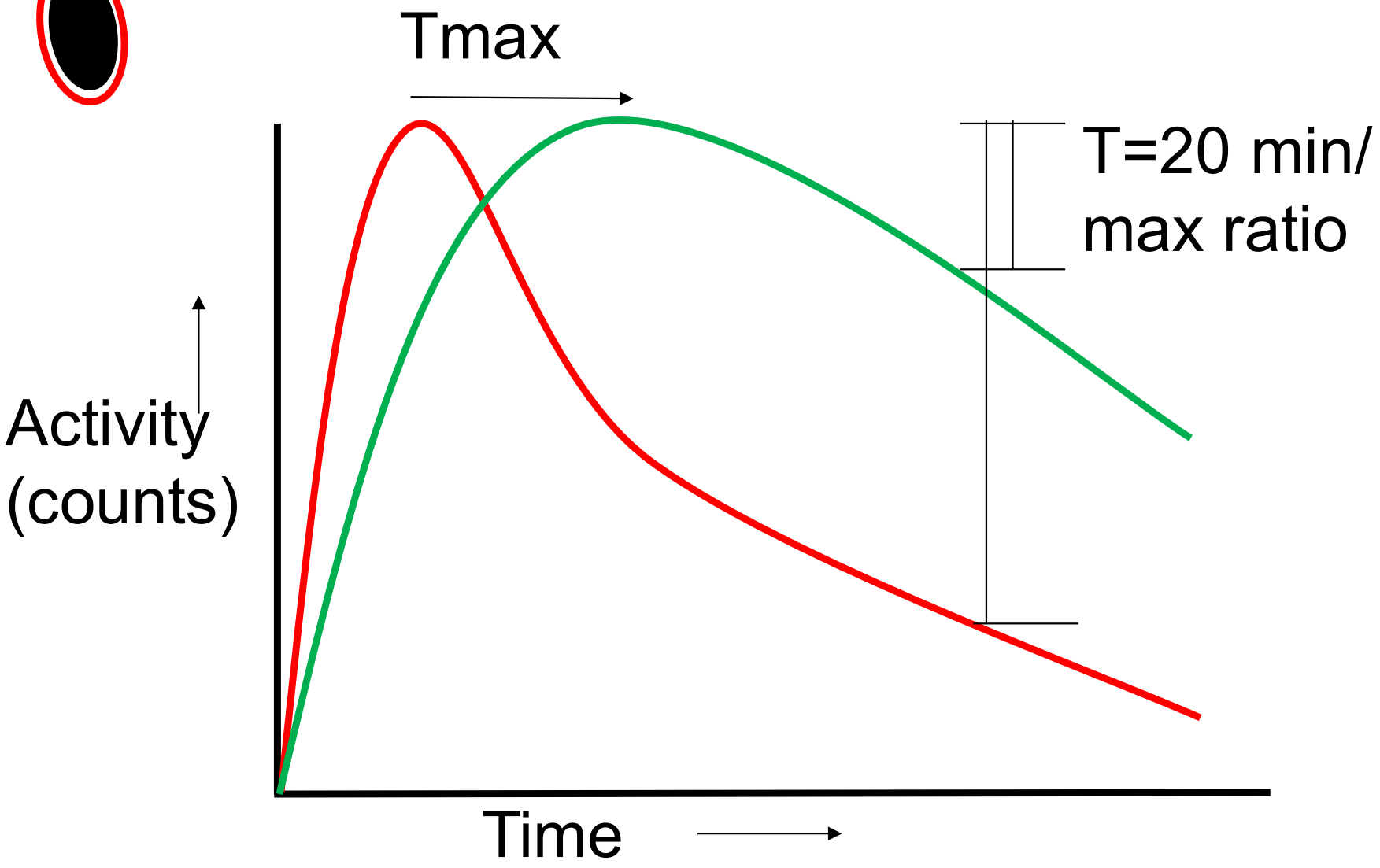

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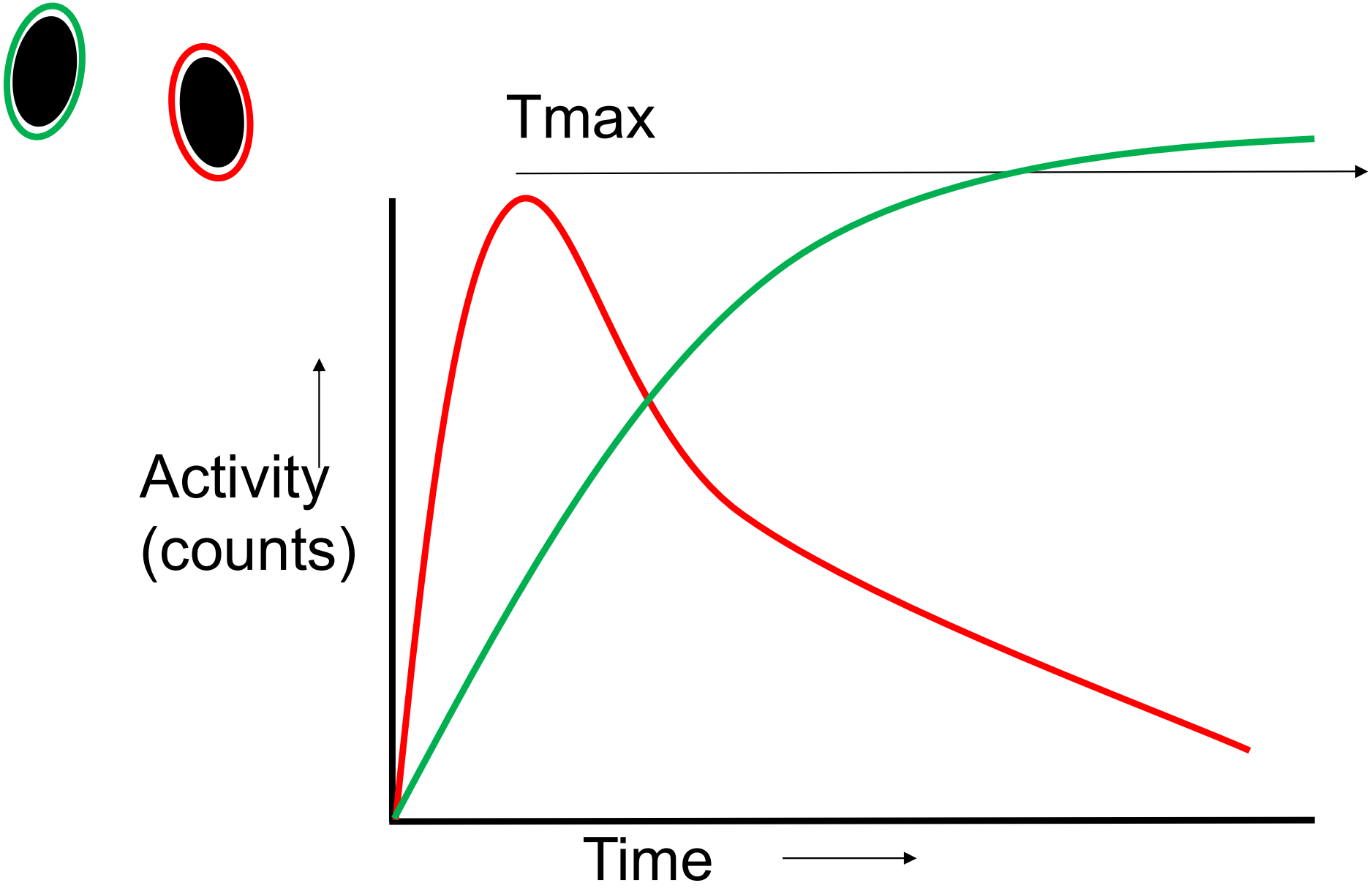

MAG3: Reference values?

- Reference values for MAG3 time activity curve not well-described
- When is Tmax too slow?
- When is excretion (e.g. 20 min / max ratio) too slow?
- Could vary with age (age dependent reference values are even less well described)

MAG3: history – reference values

Comparison of Iodine-131 OIH and Technetium-99m MAG_3 Renal Imaging in Volunteers

Andrew Taylor, Jr., Dennis Eshima, Alan R. Fritzberg, Paul E. Christian, and Sudhakar Kasina

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J Nucl Med 27:795–803, 1986

TABLE 5
Time (sec) to Maximal Activity [^{99m}Tc]MAG_3 and OIH Using Both Cortical and Whole Kidney Regions of Interest

Subject		Whole kidney ROI		Cortical ROI	
		MAG_3	OIH	MAG_3	ROI
1-S	L	125	125	105	105
	R	125	225	125	225
2-E	L	445	—	187	—
	R	245	—	165	—
3-R	L	185	405	145	165
	R	405	245	165	165
4-Do	L	165	185	165	185
	R	165	245	165	145
5-Hn	L	345	305	185	165
	R	225	285	165	185
6-Hs	L	145	265	125	145
	R	145	205	125	125
7-De	L	285	245	145	125
	R	265	225	145	145
8-C	L	185	185	145	165
	R	285	185	165	165
9-B	L	145	165	125	165
	R	165	205	165	185
10-W	L	145	145	125	145
	R	225	165	125	145
Mean ± s.d.		207 ± 80	223± 66	145 ± 22	158 ± 27

Aim of the study

To establish reference ranges for often-used and easily determinable renography parameters in a large number of patients subdivided in age groups.

Methods

- Retrospective study, Jan 1, 2014-July 31, 2017

- Evaluated 745 MAG3 procedures

- Excluded patients:
  - Systemic disease affecting kidney function
  - Disease / anatomy bilaterally affecting kidneys
  - History of urogenital pathology
  - History of radiation therapy / surgery to urogenital system
  - No history available
  - GFR <60 ml/min/1,73 m^2

- Excluded single kidneys:
  - Disease / anatomy unilaterally affecting kidney (contralateral normal kidney was included in analysis)
  - Kidney with <40% relative function

Methods

- Included 247 patients:
  - 138 right kidneys
  - 147 left kidneys

- Age 25 days – 88 years

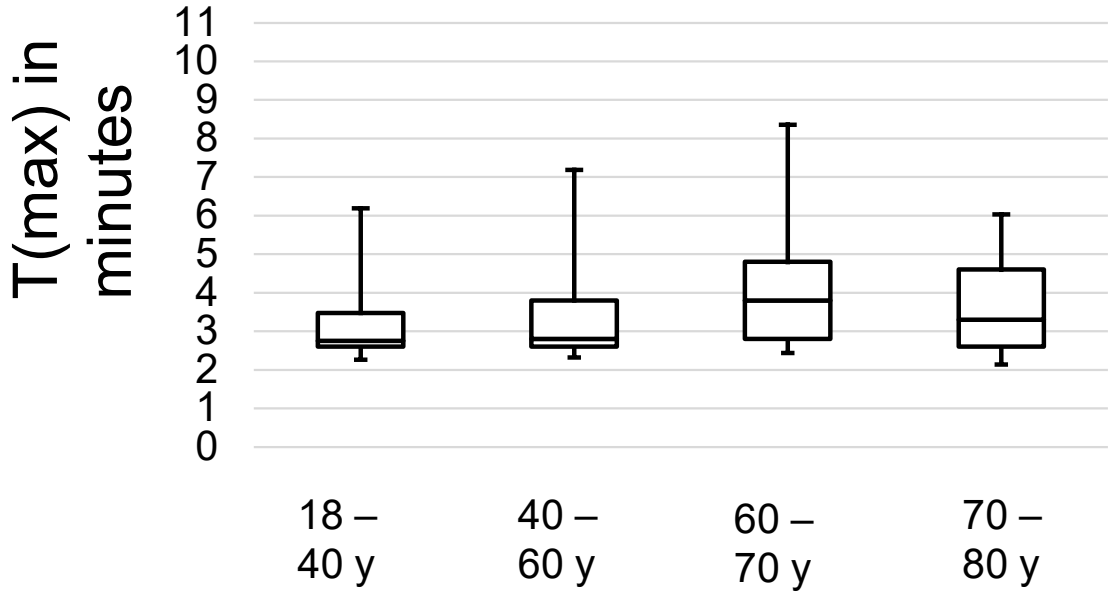
Methods: MAG3

- MAG3 injection
- Planar acquisition, dorsal view, over 30 mins p.i.
- Quanitification in time-activity curves by manually drawn ROIs, background ROI in the abdomen caudally from left kidney
- Interim evaluation after 15 minutes: furosemide challenge 1 mg / kg or 20 mg, whichever is smaller
- In patients receiving furosemide challenge: healthy kidney only included in Tmax analysis not 20 min / max ratio
- Micturation after 30 mins, then spot image acquisition in dorsal view approx. 45 min. p.i.

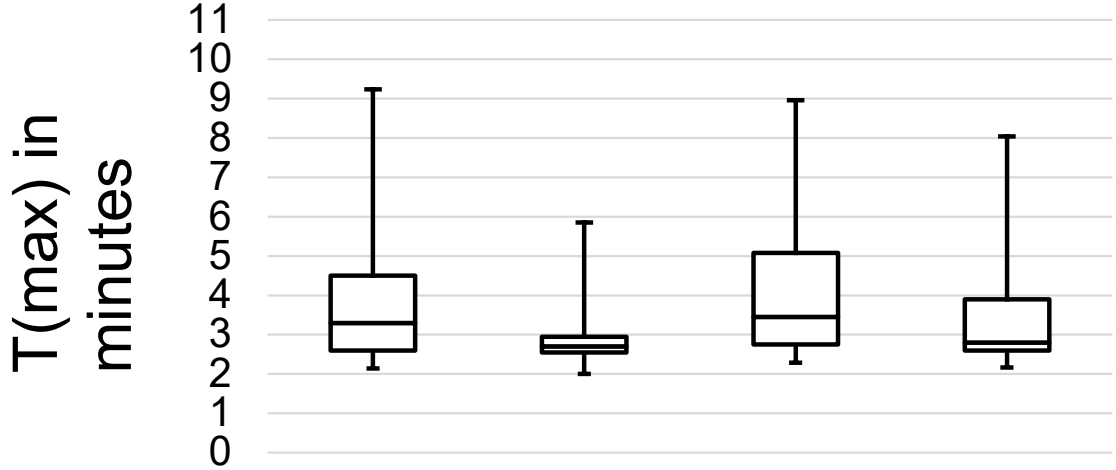
Analysis

- 6 age categories:
  - 0-0.5 years (only Tmax, too few patients for 20 mins / max ratio)
  - 0.5-2 years (only Tmax, too few patients for 20 mins / max ratio)
  - NO 2-18 years (insufficient nr. of patients)
  - 18-40 years
  - 40-60 years
  - 60-70 years
  - 70-80 years

Tmax: right vs. left

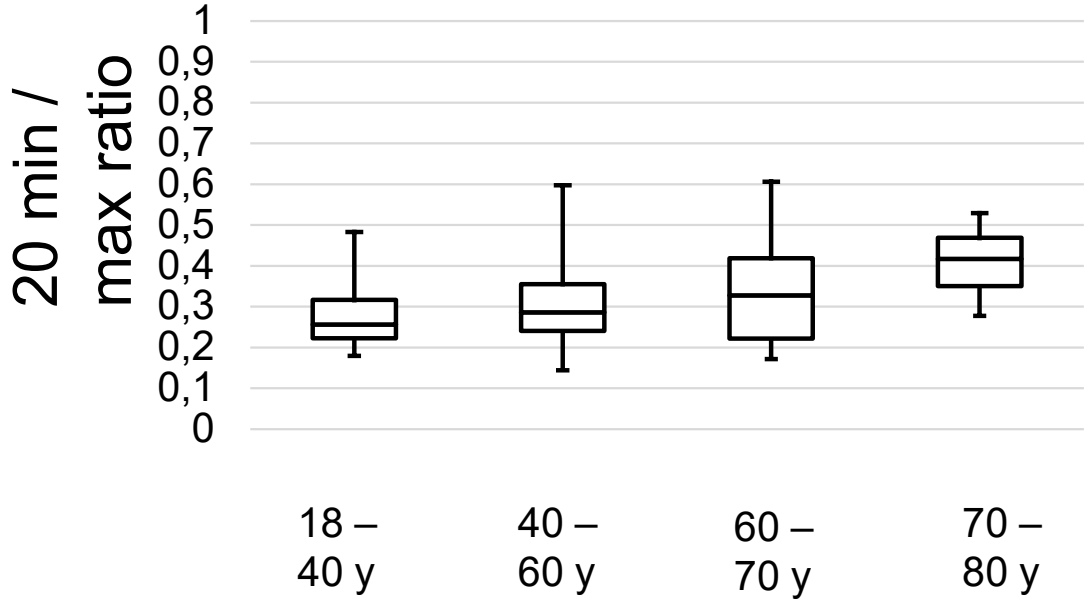


Right kidneys

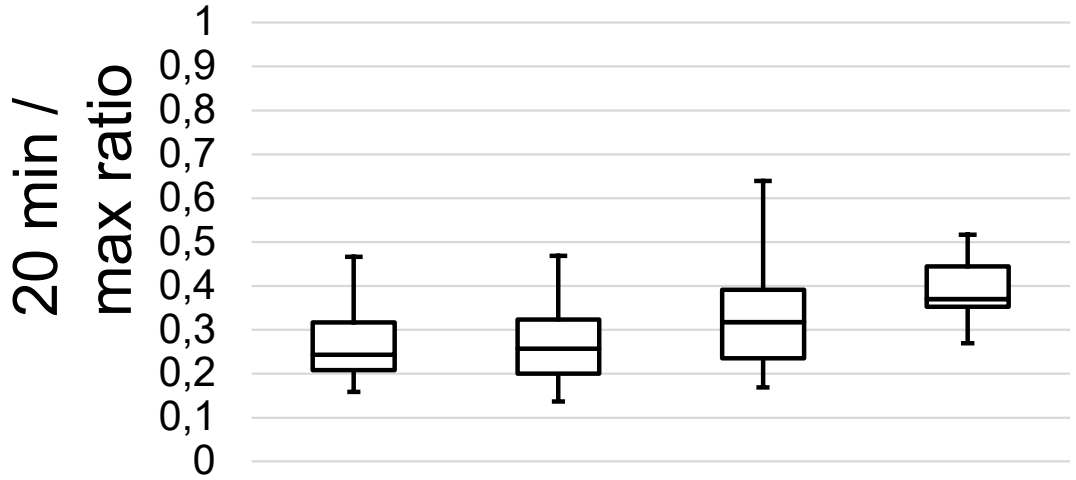


Left kidneys

20 min / max ratio



Right kidneys



Left kidneys

Reference values: all adults

Table 1. Reference values for T(max) and 20 min/T(max) count ratio of MAG3 scintigraphy for adults

Adults		N	M	SD	Percentile 2,50%	Percentile 25%	Percentile 50%	Percentile 75%	Percentile 97,5%
T(max)	Right kidney	138	3,65	1,49	2,2	2,6	3,0	4,3	7,4
	Left kidney	147	3,54	1,64	2,0	2,6	2,8	4,0	8,5
20 min/T(max) count ratio	Right kidney	106	0,33	0,11	0,16	0,24	0,31	0,40	0,59
	Left kidney	118	0,31	0,11	0,16	0,23	0,30	0,38	0,57

Reference values: all adults

Table 4. Reference values of T(max) for the right and left kidney in age categories for children

Childre n		N	Percentile 2,5%	Percentile 25%	Percentile 50%	Percentile 75%	Percentile 97,5%
T(max) right kidney	0-0.5 y	20	2,30	2,55	2,86	5,25	9,31
	0.5-2 y	16	1,95	2,38	2,80	3,78	10,05
T(max) left kidney	0-0.5 y	7	1,78	2,25	2,60	4,75	5,00
	0.5-2 y	5	2,71	2,80	3,90	4,00	6,61

Reference values: T-max

Table 2. Reference values of T(max) for the right and left kidney in age categories

		N	Percentile 2,5%	Percentile 25%	Percentile 50%	Percentile 75%	Percentile 97,5%
T(max) right kidney	18-40 y	22	2,26	2,60	2,75	3,48	6,19
	40-60 y	50	2,32	2,60	2,80	3,80	7,19
	60-70 y	33	2,44	2,80	3,80	4,80	8,36
	70-80 y	29	2,14	2,60	3,30	4,60	6,03
T(max) left kidney	18-40 y	25	2,14	2,60	3,30	4,50	9,24
	40-60 y	59	2,00	2,55	2,70	2,95	5,86
	60-70 y	34	2,28	2,75	3,45	5,08	8,96
	70-80 y	25	2,16	2,60	2,80	3,90	8,04

Reference values: 20 min / max ratio

Table 3. Reference values of 20 min/T(max) count ratio for the right and left kidney in age categories

		N	Percentile 2,5%	Percentile 25%	Percentile 50%	Percentile 75%	Percentile 97,5%
20 min/mx count ratio right kidney	18-40 y	19	0,18	0,22	0,26	0,32	0,48
	40-60 y	42	0,14	0,24	0,29	0,35	0,60
	60-70 y	22	0,17	0,22	0,33	0,42	0,61
	70-80 y	20	0,28	0,35	0,42	0,47	0,53
20 min/mx count ratio left kidney	18-40 y	18	0,16	0,21	0,24	0,32	0,47
	40-60 y	52	0,14	0,20	0,32	0,32	0,47
	60-70 y	24	0,17	0,24	0,32	0,39	0,64
	70-80 y	21	0,27	0,35	0,37	0,44	0,52

P<0.001

P=0.006

Reference values: Literature Tmax

Table 5. Comparison of the determined reference values of T(max) from MAG3-scintigraphs of adults with the literature

Studies			N	M	SD	Min	Max
Esteves et al. 2006	Men	Right kidney	44	3,6	2,1	2,1	15,3
		Left kidney	44	3,2	1,0	2,1	6,3
	Women	Right kidney	62	4,4	2,7	2,3	16,3
		Left kidney	62	3,7	1,7	2,3	11,3
Clausen et al. 2002		Single kidney	74	3,1	0,6	1,9	5,3
Lin et al. 1998		Right kidney	162	3,8	1,1		
		Left kidney	162	3,6	1,1		
Klingensmith et al. 1994		Right kidney	36	3,8	2,3		
		Left kidney	36	3,3	2		
Present study		Right kidney	138	3,7	1,5	2	10,4
		Left kidney	147	3,5	1,6	1,9	10,5

Reference values: Literature Tmax

Table 6. Comparison of the determined reference values of 20 min/T(max) count from MAG3-scintigraphs of adults with the literature

Studies		N	M	SD	Min	Max
Esteves et al. 2006	Right kidney	106	0,24	0,14	0,11	0,96
	Left kidney	106	0,22	0,08	0,11	0,61
Clausen et al. 2002	Single kidney	74	0,22	0,05	0,09	0,33
Our results	Right kidney	106	0,33	0,11	0,09	0,66
	Left kidney	118	0,31	0,11	0,09	0,7

Discussion

- Gender analysis: no difference male vs. female
- Difficulties:
  - What is a “normal” kidney (there was a reason for referral) – hidden anomalies cannot completely be excluded in spite of “normal” assessment
  - Insufficient nr. of patients 2-18 years

Overall conclusions / take home message

- True “reference range” difficult to measure considering large number of health volunteers necessary and values are derived from patients already referred for MAG3-scintigraphy

- Normal values:
  - Tmax: median 3 minutes, 95% reference interval 2-8 minutes, no real age dependency
  - 20 min / max ratio: 0.32, 95% reference interval 0.24-0.58, older patients have significantly lower ratio (slower clearance)

Thank you for your attention!