Innovations in Evaluations & Management of Renal Complications in ADPKD

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COI

- **Investigator of TEMPO study, research funding from Otsuka**

Challenges in the Evaluations & Management of Renal Complications in ADPKD

- Kidney cyst infections
- Chronic Pain

Challenges of kidney cyst infections in ADPKD

Difficulty in diagnosis

- **Fever and abdominal pain carries a broad differential.**
- **Conventional imaging may not be definitive in**
  - **isolating the location of infection**
  - **differentiating cyst infection from cyst hemorrhage or pyelonephritis.**
- **Blood and Urine culture is often negative.**
  - *Urine and blood cultures were found to be respectively positive in 39 and 24% episodes.*

Clin J Am Soc Nephrol 2009; 4: 1154–1155
Clin J Am Soc Nephrol 2009; 4: 1183–1189

Challenges of kidney cyst infections in ADPKD

Difficulty in Treatment

- Empiric therapy with antibiotics that is widely known to penetrate cyst
- Infection recurs after antibiotic treatment discontinuation
- Percutaneous or surgical drainage of infected cysts required
  - 5/33 pts for cyst drainage, 4/33 extirpation (nephrectomy or partial hepatectomy)

Clin J Am Soc Nephrol 4: 1154–1155, 2009.
Clin J Am Soc Nephrol 4: 1183-1189, 2009

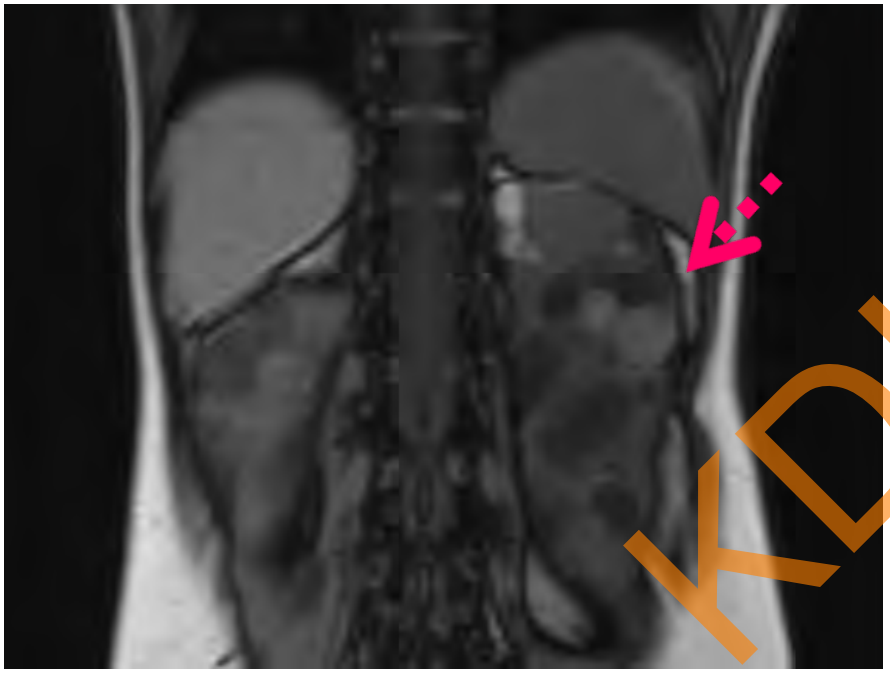
Case 19F

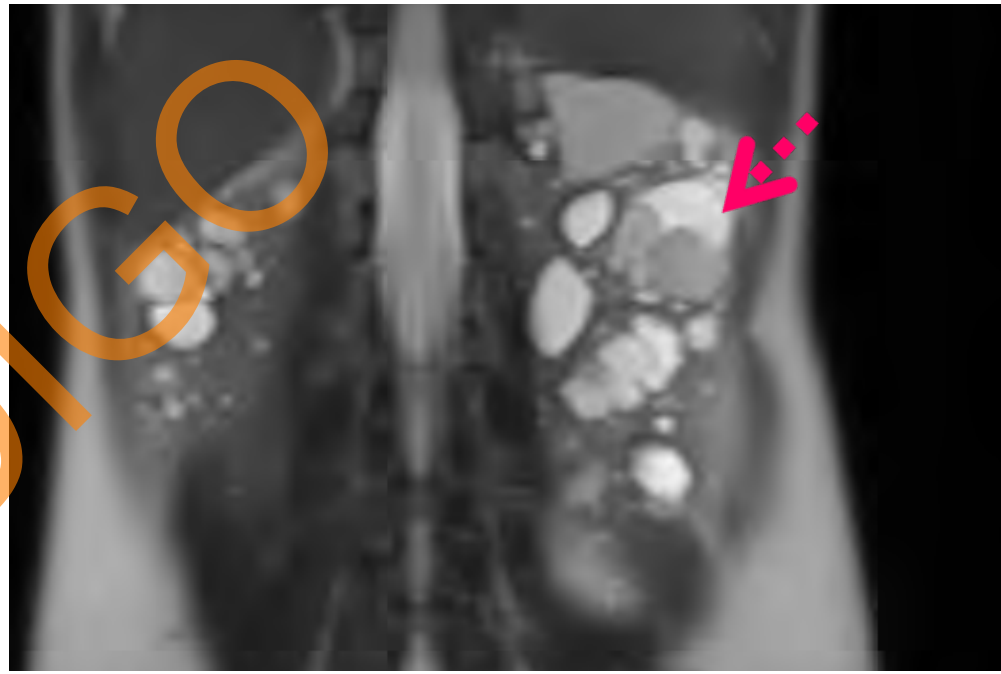
Present illness:

- 5 episodes of high fever within 6 months.
- Treated with antibiotics and puncture/drainage of the cysts.
- Referred to us after the last episode of fever.
  - WBC 11700/mm3, Cr 0.66 mg/dl, CRP 7.12 mg/dl
  - Urine WBC 50-99/HPF, RBC 20-29/HPF
  - Urine culture from previous hospital: Citrobacter diversus

Family History: Father : ESRE with ADPKD

June 2012

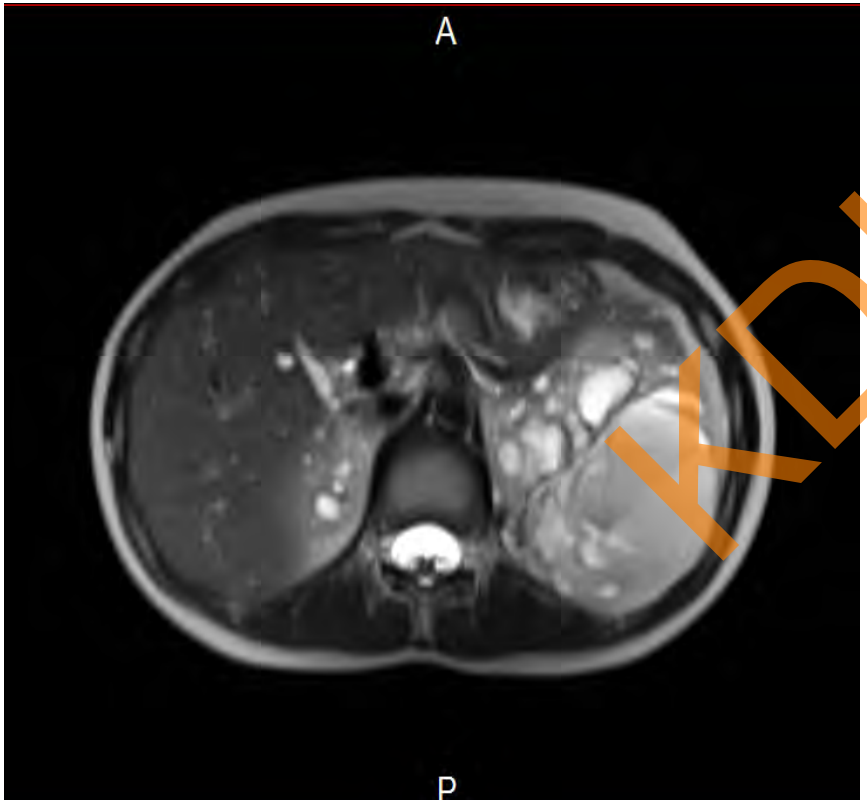


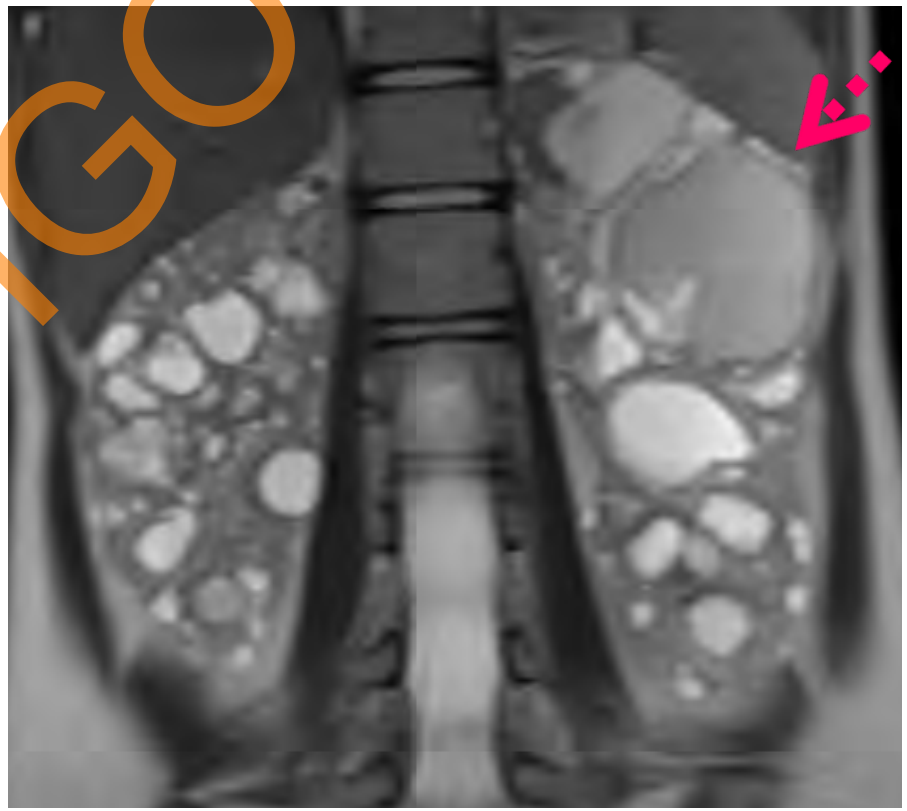


Case 19F

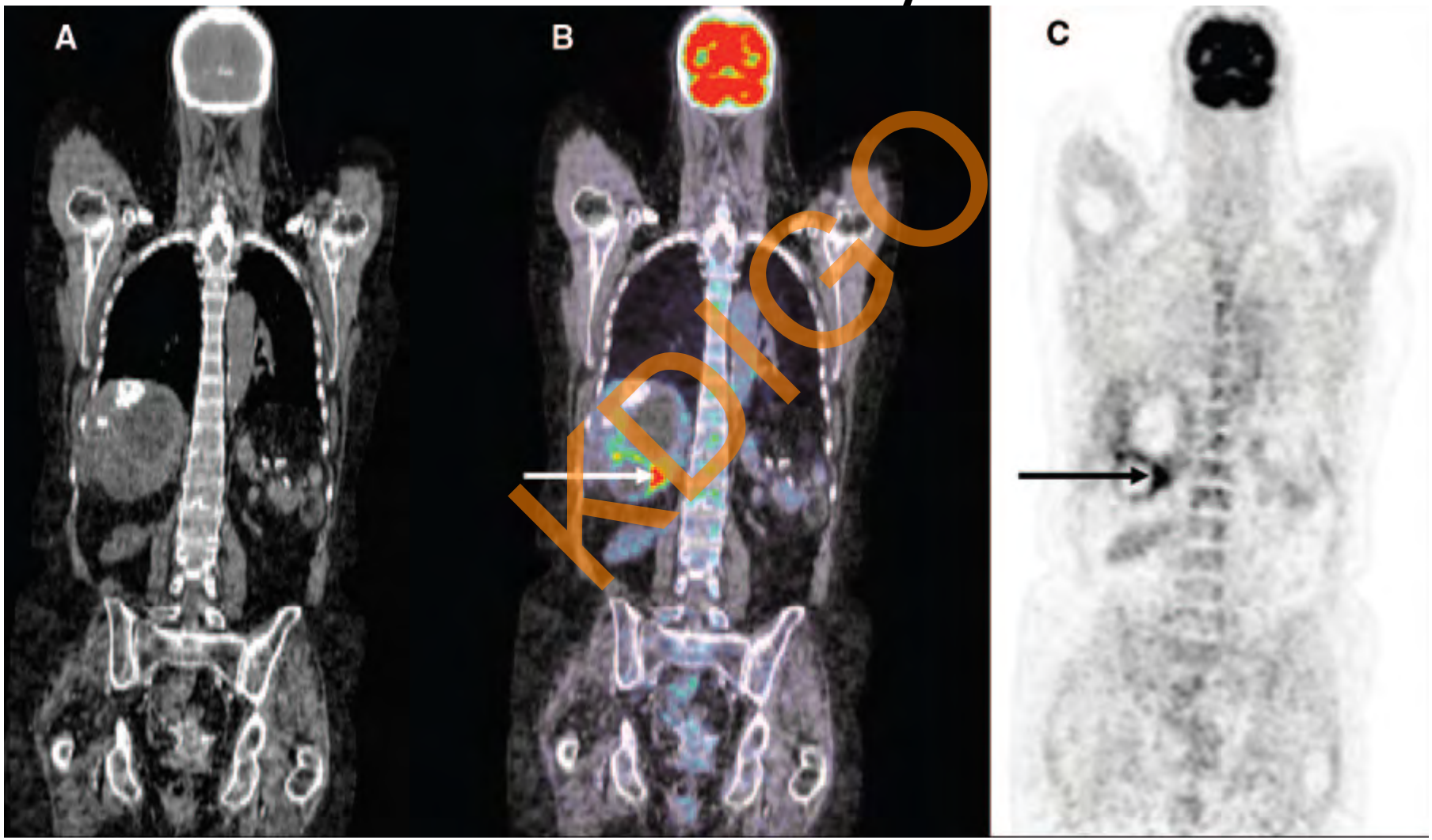
1. Her temperature went down with carbapenem, although her infection recurred after the discontinuation of the treatment.
2. Laparoscopic marsupialization of the infected cysts were planned.
    i. Construct 3D image and 3D model of the kidney
    ii. CT-guided puncture of the cyst and instillation of methylene blue
    iii. Laparoscopic marsupialization

Sep. 2012



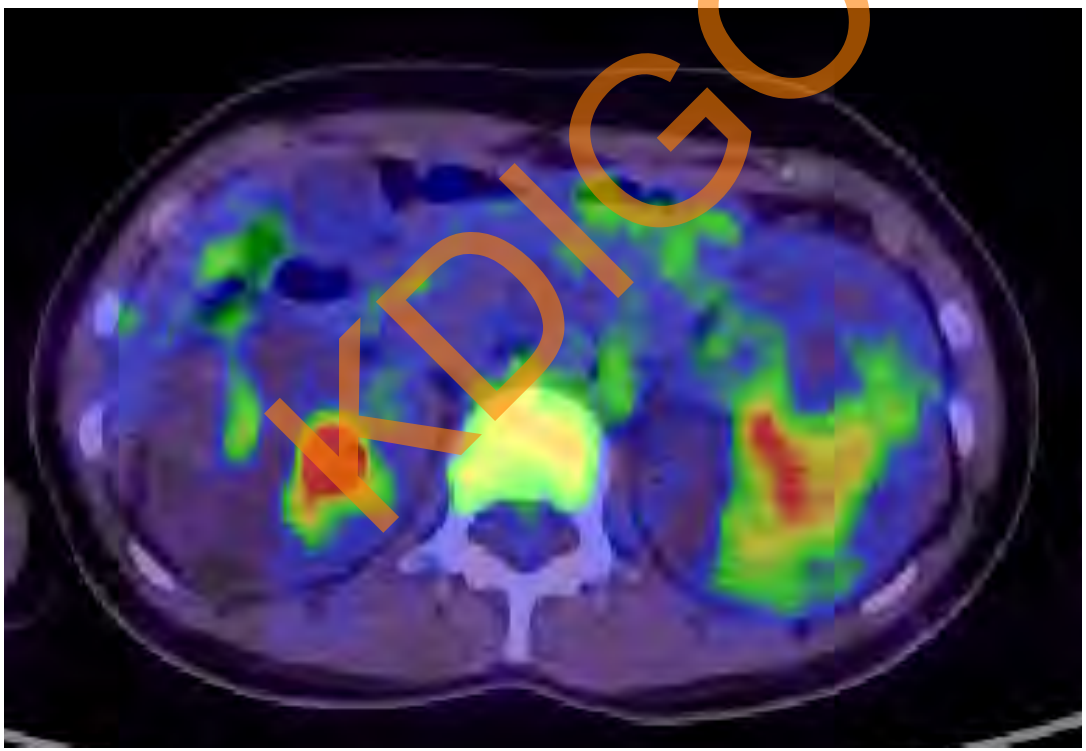


^{18}FDG PET/CT for the diagnosis of infectious cysts

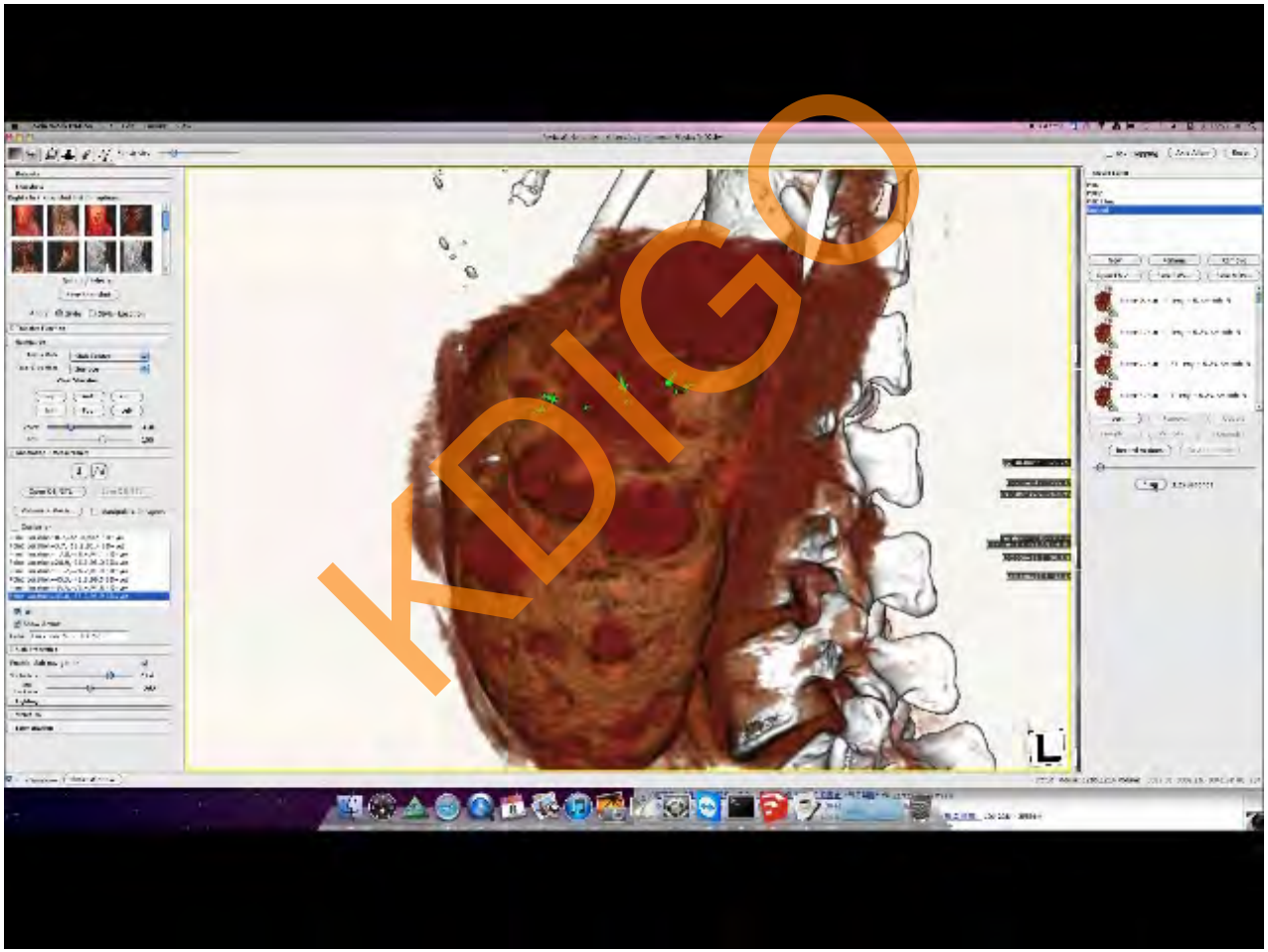


Clin J Am Soc Nephrol 6: 1644–1650, 2011.

Dec 2012



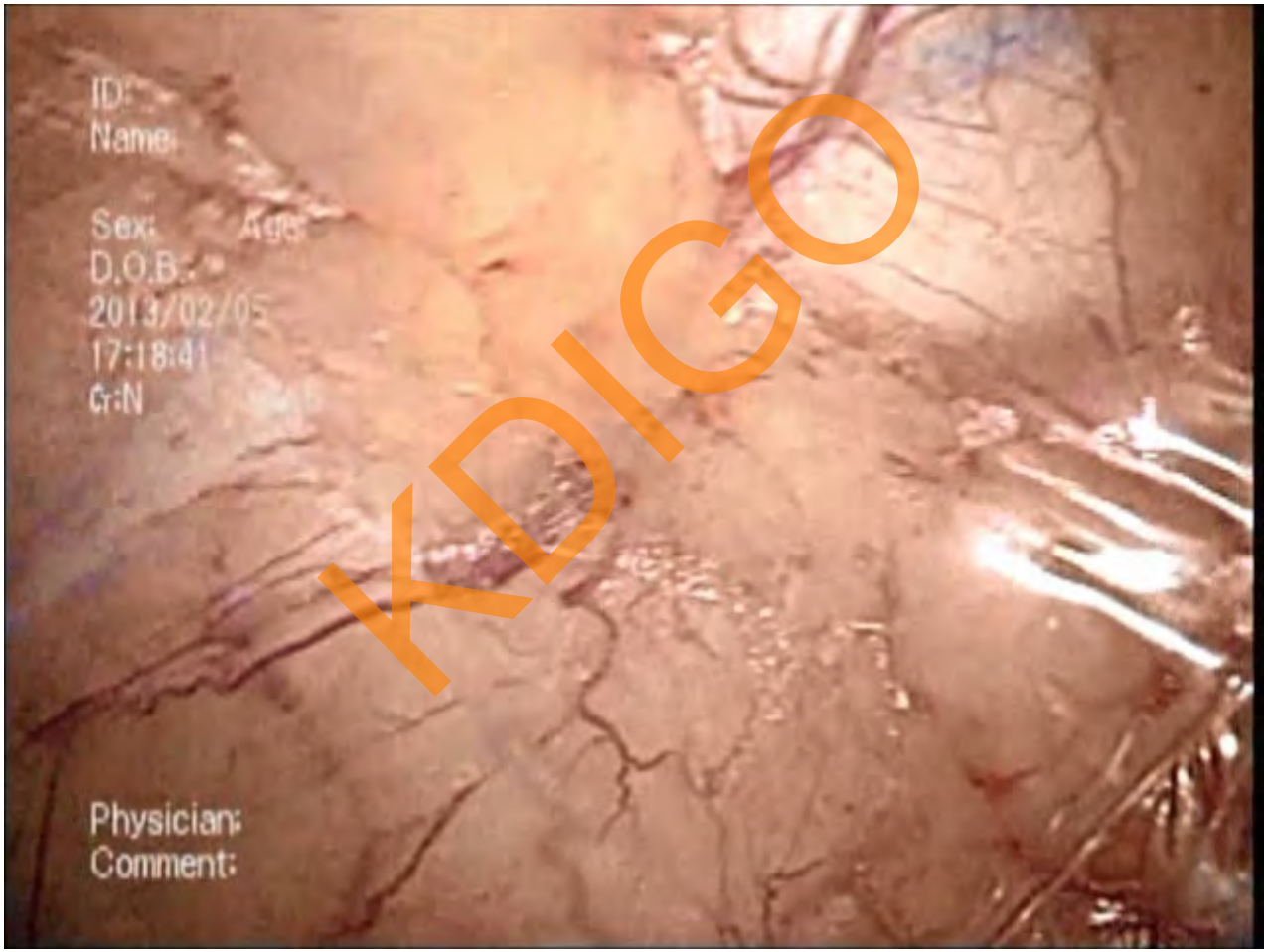
3D navigation of renal cysts




KDIGO

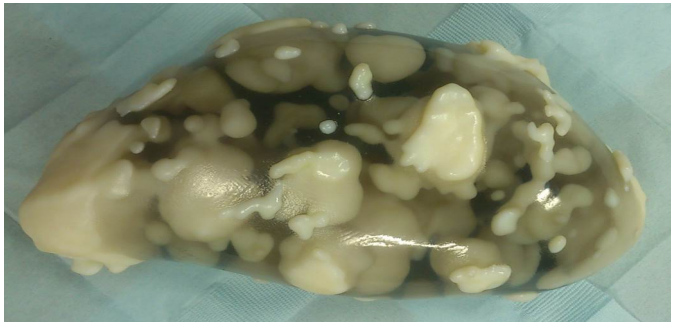
3D model of the kidney made of 3D printer

Laparoscopic marsupialization



Construction of 3D model has advantages in

- Explanation of the disease and the procedure to the patient and family
- Identifying the precise location of the cysts and the simulation of surgery



Challenges in the Evaluations & Management of Chronic Pain in ADPKD

- **Chronic pain is a common complaint…, with a negative impact on sleep, activity, mental status, and social relationships .**

  – *Pain Manag Nurs 2009;10:134–141.*

- **Chronic pain is one of the most difficult symptoms to treat.**

  – Adv Chronic Kidney Dis 2010;17:e1–e16.

A sequential approach to pain management in ADPKD

- Non-pharmacologic therapies
- Systemic, non-narcotic analgesics
- Low-dose opioids
- Transcutaneous electrical nerve stimulation
- Acupuncture
- Spinal cord stimulation (neuromodulation9
- Neuraxial opioids and local anesthetics
- Surgical decortication
- Renal denervation
- Transcatheter arterial embolization

Advances in Chronic Kidney Disease, Vol 17, No 3 (May), 2010: pp e1-e16

A sequential approach to pain management in ADPKD

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Advances in Chronic Kidney Disease, Vol 17, No 3 (May), 2010: pp e1-e16

Surgical Cyst Decortication in ADPKD; review of literature

Author (year)	n	Follow-up periods	50% pain relief	100% pain relief
Haseebuddin (2012)	18	Mean; 130 M	8/12 (67%)	
McNally (2003)	7	Mean; 14 M	5/7 (71%)	2/7 (29%)
Lee (2003)	29	Mean; 32 M	73% (at 12 months)	
			52% (at 24 months)	
			81% (at 36 months)	
Lifson (1998)	7	Mean; 26 M		5 (71%)
Elashry (1996)	5	3-15 M	5/5 (100%)	1/5 (20%)
Brown (1996)	8	12-28 M	5/8 (63%)	5/8 (63%)
Teichman (1995)	6	6-40 M		5/6 (83%)
Elzinga (1992)	26	21±2	80% (at 12 months)	
			62% (at 24 months)	
Chehval (1995)	3	16 M		3/3 (100%)

Surgical Cyst Decortication in ADPKD

- **Cyst decortication in patients with ADPKD has a long history.**
  - *Rovsing T. Treatment of multilocular renal cyst with multiple punctures. Hospitalstid 1911;4.*
  - *Teichman J, Hulbert J. Laparoscopic marsupialization of the painful polycystic kidney. J Urol 1995;153:1105–7.*
- **Cyst decortication is highly effective in the management of disease-related chronic pain for the majority of patients with ADPKD, providing durable pain relief.**

Robotic Surgical Cyst Decortication in ADPKD

Renal denervation for chronic pain in ADPKD

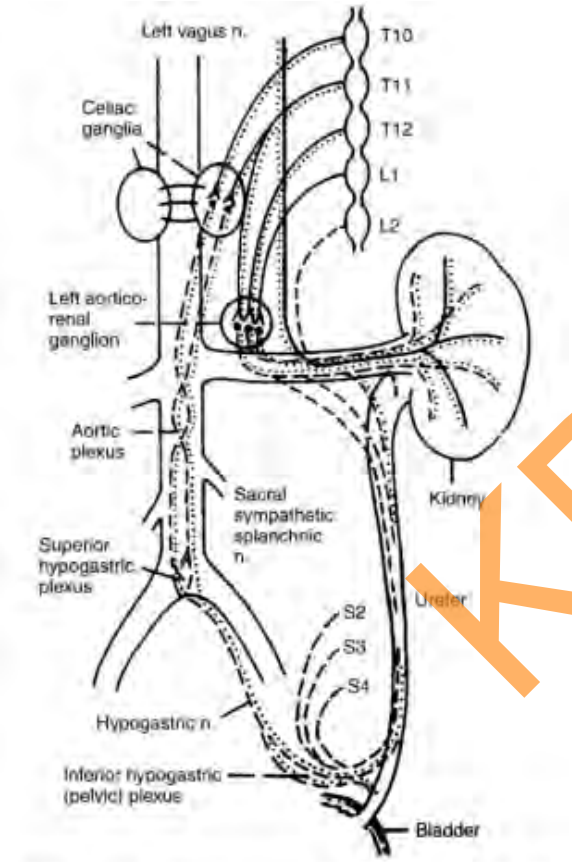
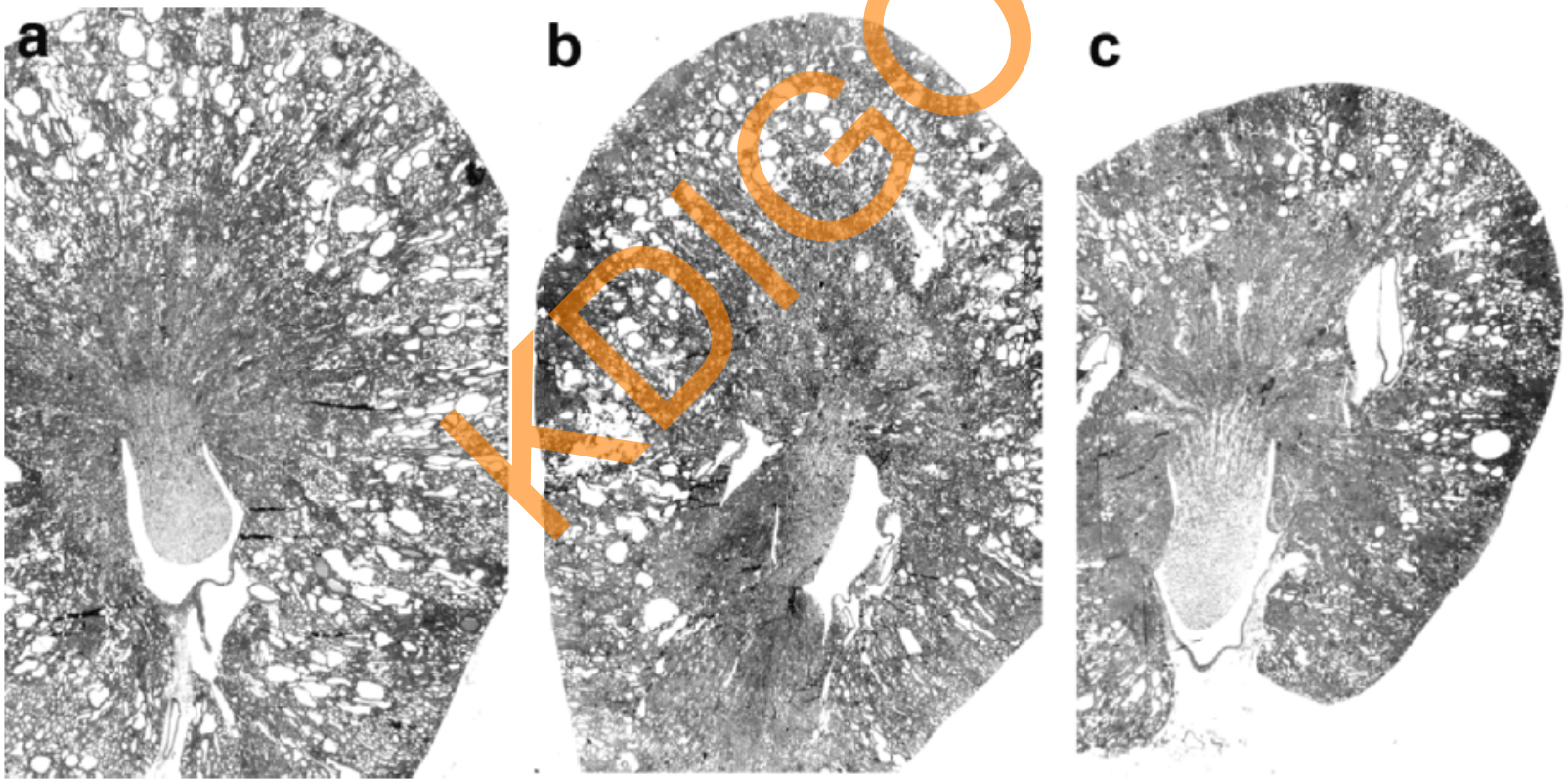


Figure 3. Innervation of kidney. Abbreviation: n., nerve. Reproduced from Bajwa et al[1] with permission of Macmillan Publishers Ltd.

- Sensory innervation of the kidney is mediated predominantly via sympathetic afferents derived from spinal segments T10 through T12.
- Afferent C fibers from the renal parenchyma and A delta fibers from the renal pelvis and calices travel along the renal artery to the renal plexus, which is composed of fibers from the celiac plexus, celiac ganglion aorticorenal ganglion, lowest splanchnic nerve, first lumbar nerve and aortic.

Renal denervation inhibits cyst growth in Cy/+ rats

Control sham bil RND



Exp Biol Med 233:952–957, 2008

Renal denervation (RND) for chronic pain in ADPKD

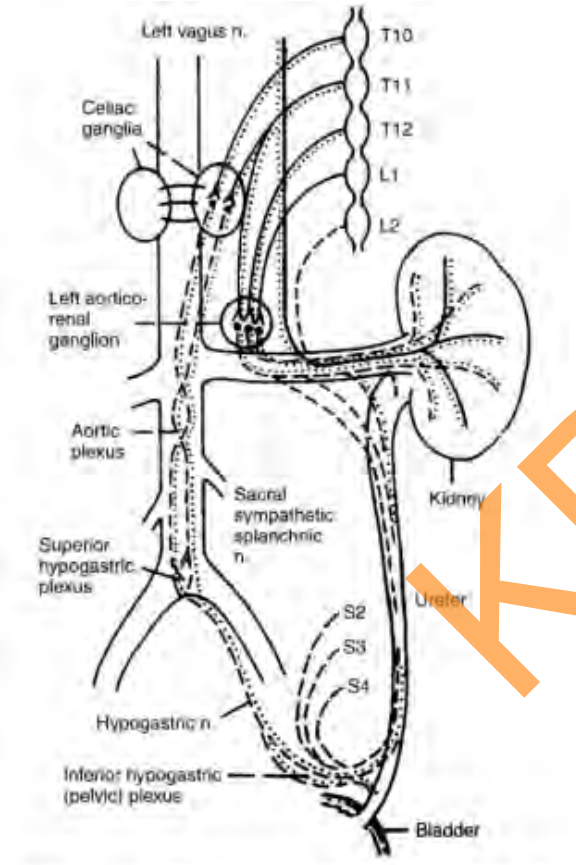


Figure 3. Innervation of kidney. Abbreviation: n., nerve. Reproduced from Bajwa et al[1] with permission of Macmillan Publishers Ltd.

- **Renal denervation for Loin pain haematuria syndrome (LPHS) related pain, with a success rate of approximately 25%.**
  - *BJU Int, **93:** 818, 2004*
  - *Br J Urol, **80:** 6, 1997*
- **Laparoscopic renal denervation made 4 adolescent ADPKD pts pain free**
  - *J Urol 175, 2274-2276, June 2006*

Renal denervation (RND) by percutaneous radiofrequency ablation (RF) for refractory hypertension

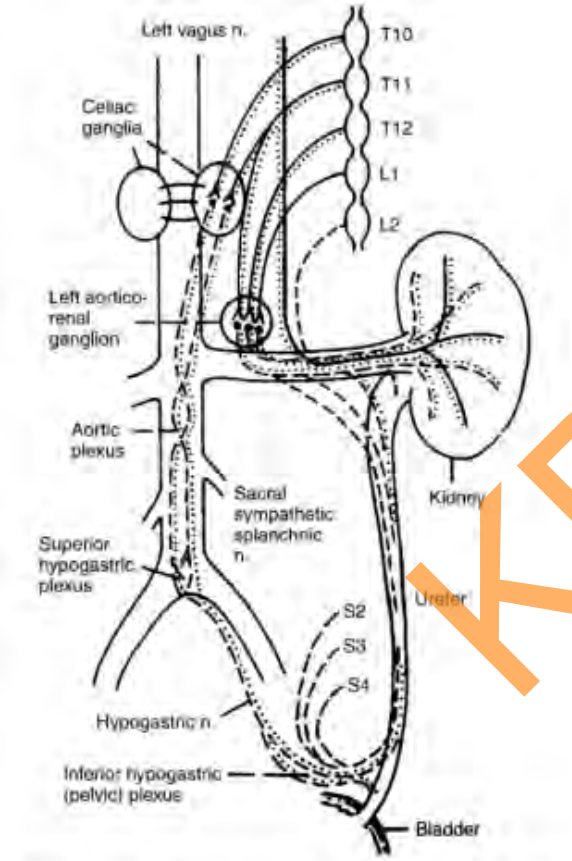


Figure 3. Innervation of kidney. Abbreviation: n., nerve. Reproduced from Bajwa et al[1] with permission of Macmillan Publishers Ltd.

- **RND by RF has been associated with reductions in blood pressure.**
  - *Lancet* 2010; **376:** 1903–09.
  - *Hypertension* 2011; **57:** 911–17.
  - *Circulation* 2012; **126:** 2976–82.

Percutaneous RND by RF for chronic kidney pain

- **A 40-year-old hypertensive lady with Loin pain haematuria syndrome (LPHS)**
- **Refractory pain symptoms despite the use of non-steroidal anti-inflammatory drugs, adjuvant antidepressants and opioid-like agents.**
- **Percutaneous RF applied only to the right renal artery.**
- **After a 6-month follow-up, the patient is pain free and normotensive with all drugs withdrawn.**

Nephrol Dial Transplant (2013) 28: 2393–2395

? Clinical trials for chronic pain +HTN with ADPKD

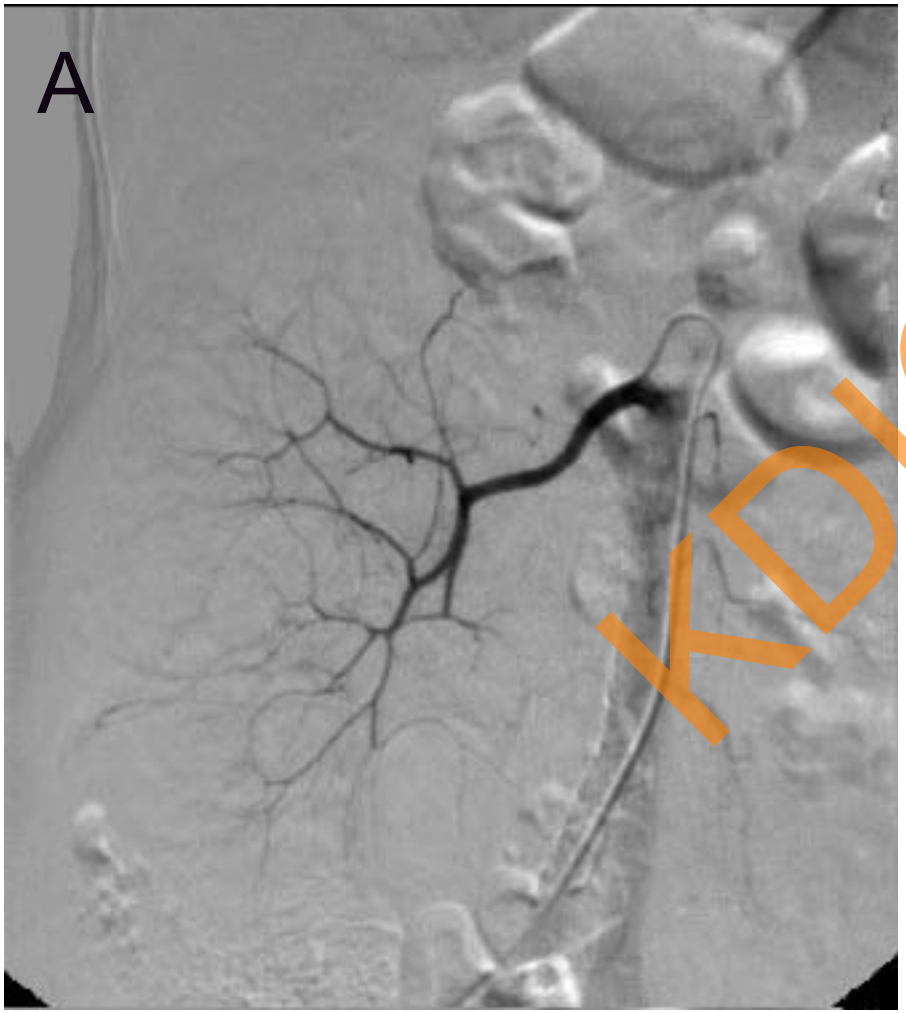
Transcatheter arterial embolization (TAE) of the renal artery

- Transcatheter arterial embolization (TAE) of the renal artery with metallic coils
- Effective and less invasive renal contraction therapy for ADPKD
- Requiremens of many metalic coils (31.2±11.2)
- Recurrence caused by recanalization and/or revascularization by collateral vessels
- Practice limited in Japan and Korea

Am J Kidney Dis 2002; 39:571–579.
Ther Apher Dial 2006; 10:333–341.

A 60-year old woman with abdominal distention

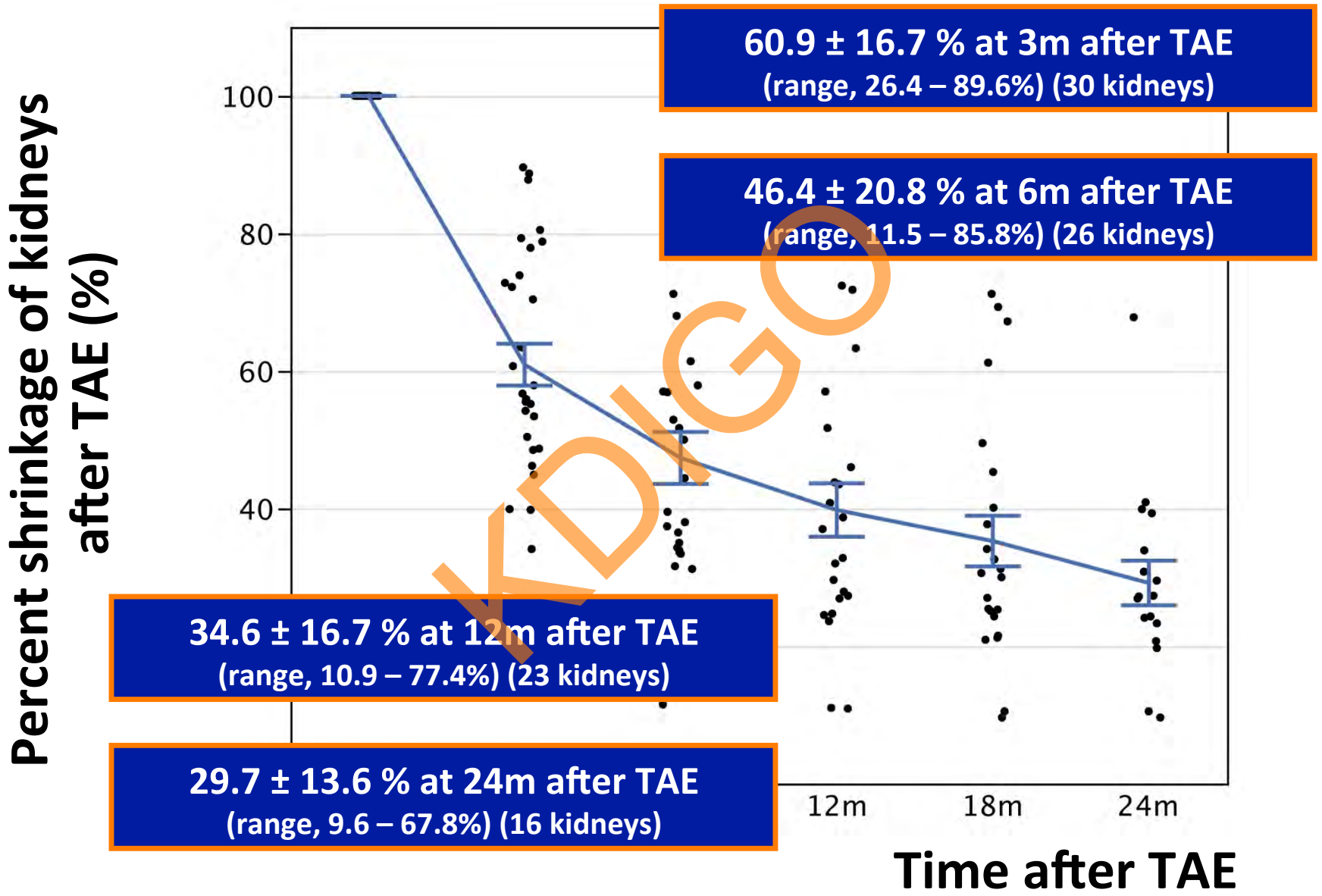
Right renal arteriogram



A. Right renal arteriogram before TAE shows narrowed andstretched renal arteries.

B. After TAE with absolute ethanol, the right renal artery is occluded.

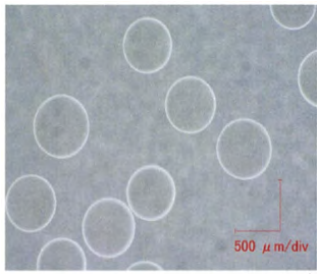
Change in kidney volume after TAE

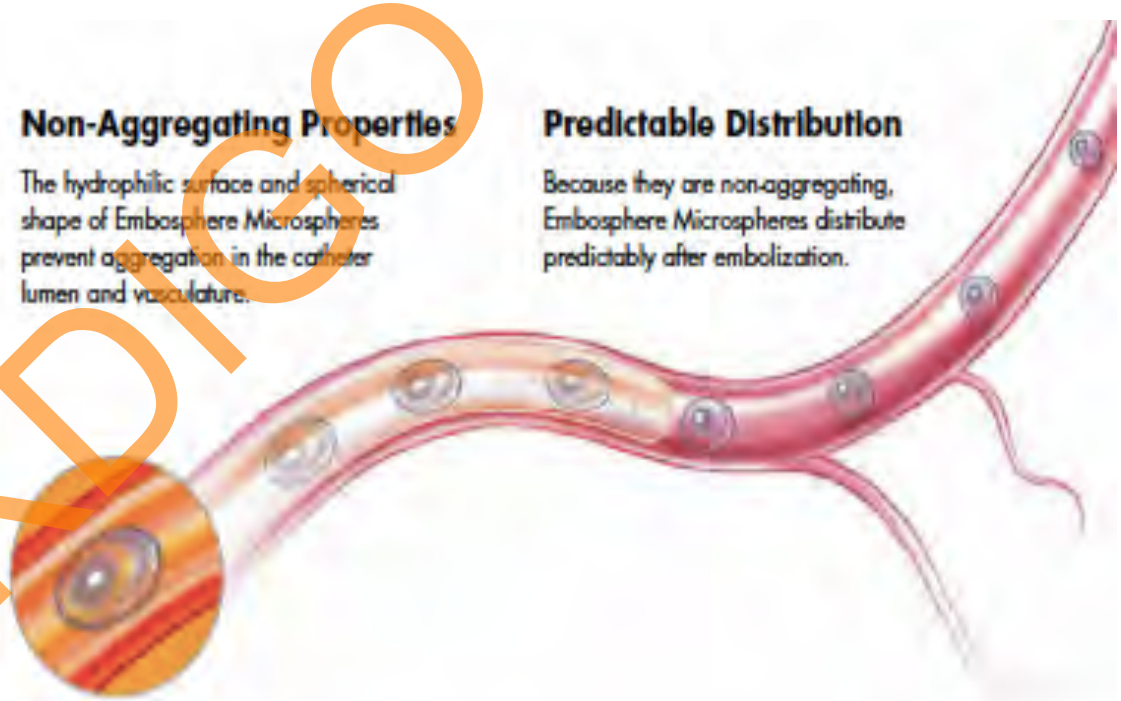


Hokkaido University Graduate School of Medicine, Department of Radiology

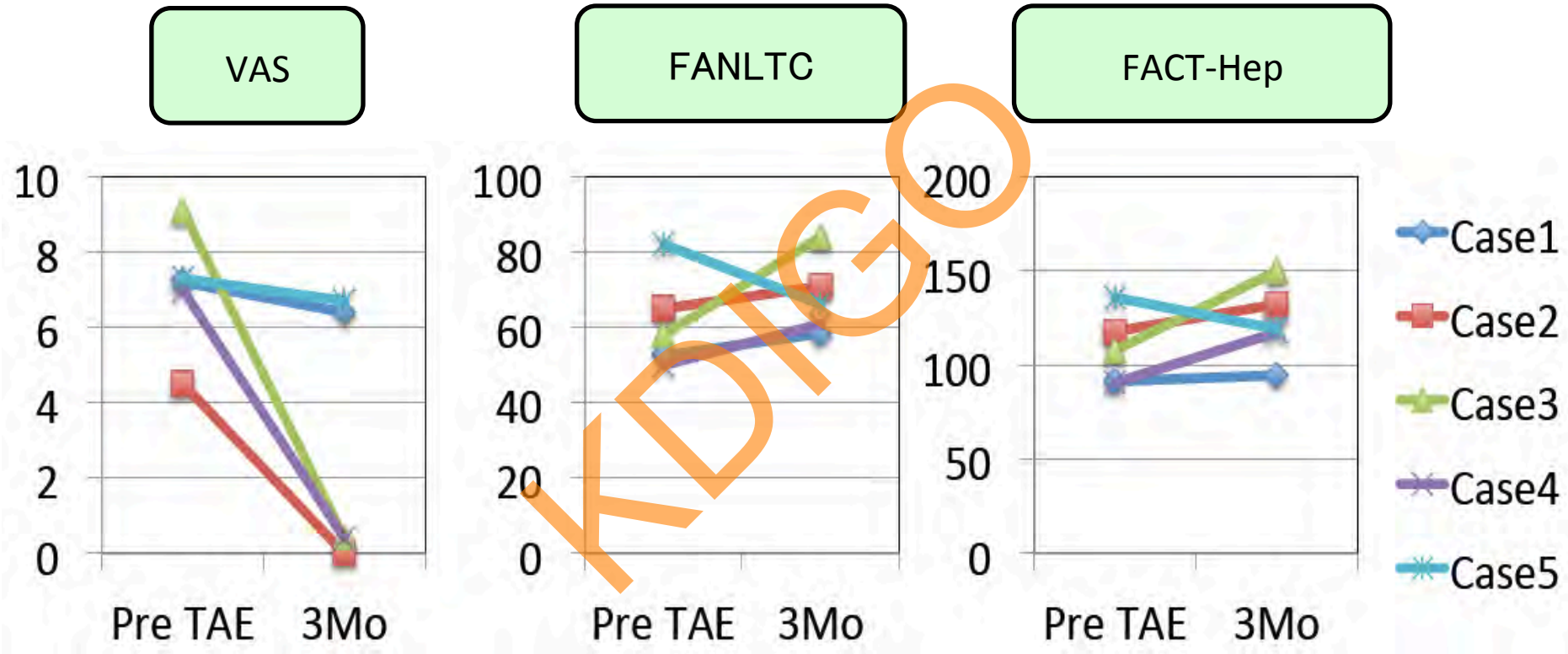
New embolic material, Embosphere®

- **Embosphere Microspheres are made from trisacryl cross linked with gelatin.**





Assessment of QOL



VAS: visual analog scale(abdominal fullness),
FANLTC: Functional Assessment of Non-Life Threatening Conditions,
FACT-Hep: Functional Assessment of Cancer Therapy-Hepatobiliary

Transcatheter arterial embolization (TAE) of the renal artery

- Significant volume reduction
- New embolic material
- ? Pain control

Innovations in the Evaluations & Management of Renal Complications in ADPKD

- Kidney cyst infections
  - Imaging; PET/CT
  - Surgical intervention; navigation for procedures
- Chronic Pain
  - Surgical decortication; mininally invasive surgery
  - Renal denervation; ? Percutaneous RND

Challenges in the Evaluations of Health-related Quality of Life in ADPKD

- HALT-PKD
- SF-36 low FRs than higher eG
- No decrea GFRs >60 than the age-m
- No report D

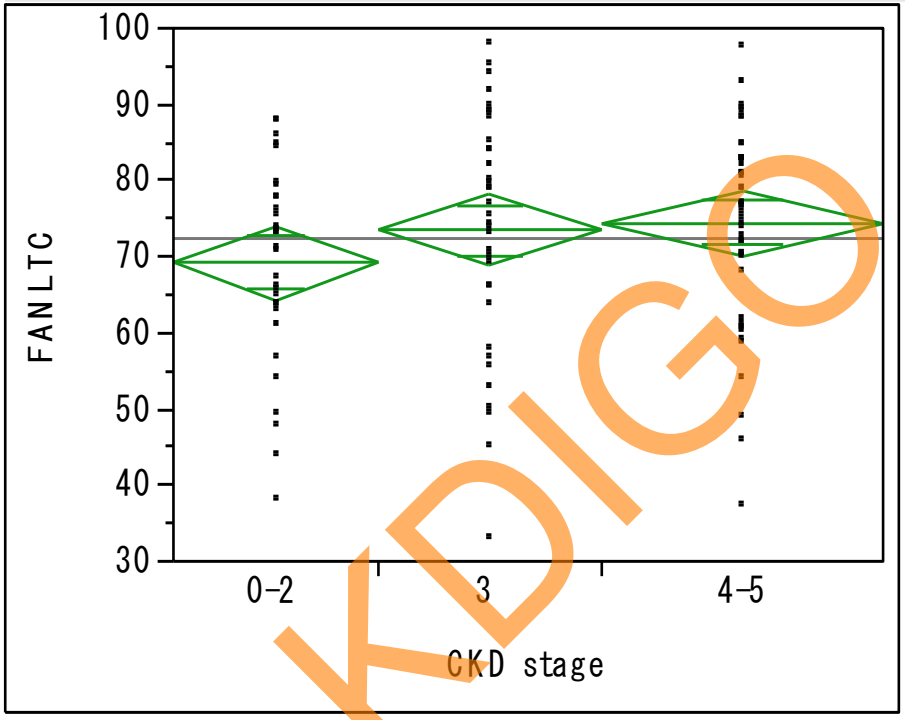
Miskulin, et al. AJKD in press

HrQOL of liver cyst

- Prospective study by Japanese consortium of PKD study, Ministry of Welfare and Health
- Case-control study (N=111)
  - Case: liver cysts occupied ≥25% of liver volume
  - Control: liver cysts <25%
- Comparison of genral (FANLTC) and liver specific QOL (FACT-Hep)

General QOL by CKD stage

CKD stageによるFANLTCの一元配置分析



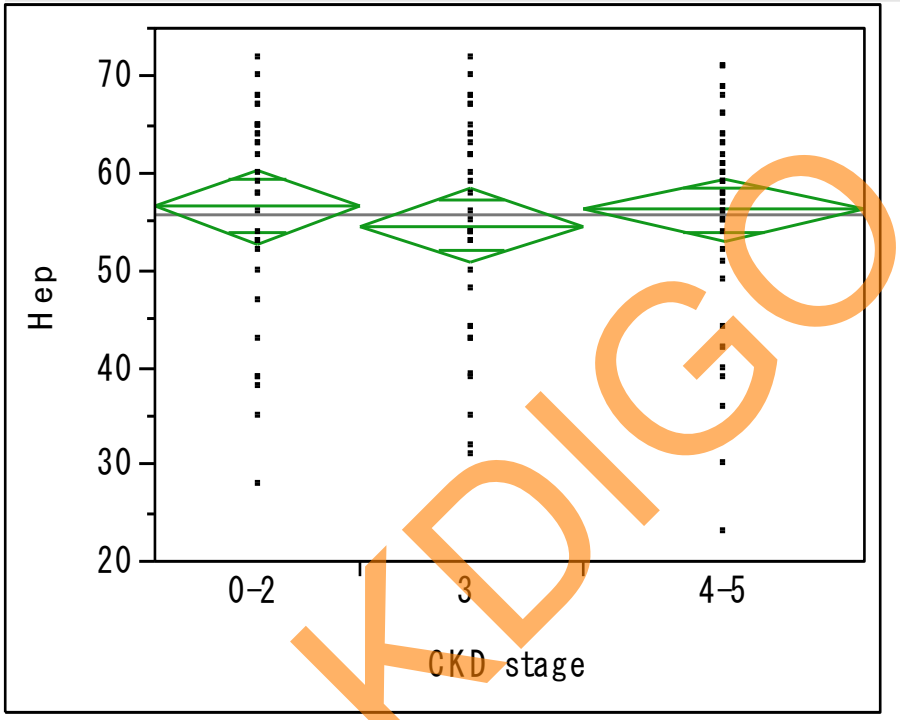
一元配置の分散分析

分散分析

要因	自由度	平方和	平均平方	F値	p値(Prob>F)
CKD stage	2	538.454	269.227	1.3997	0.2511
誤差	108	20772.954	192.342		
全体(修正済み)	110	21311.408			

Liver specific QOL by CKD stage

CKD stageによるHepの一元配置分析



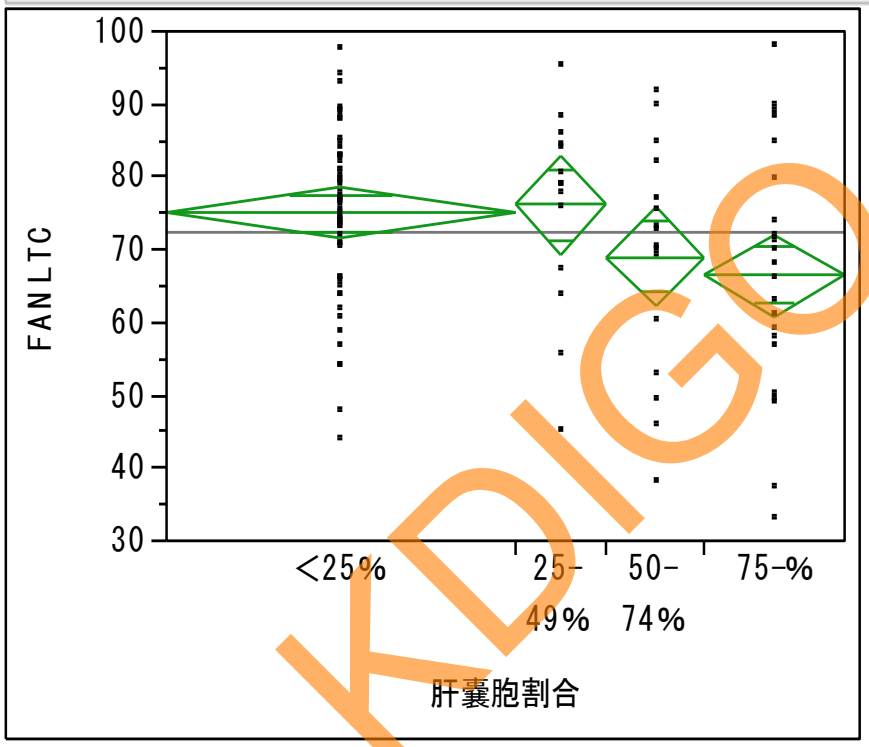
一元配置の分散分析

分散分析

要因	自由度	平方和	平均平方	F値	p値(Prob>F)
CKD stage	2	74.203	37.101	0.2979	0.7430
誤差	108	13452.288	124.558		
全体(修正済み)	110	13526.491			

General QOL by % of liver cysts occupancy

肝嚢胞割合によるFANLTCの一元配置分析



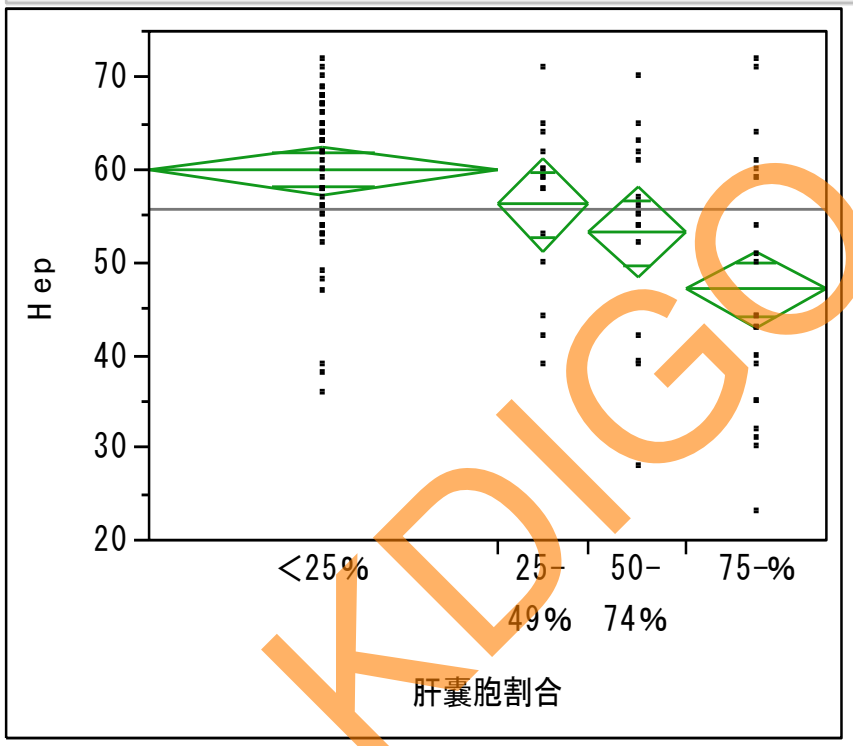
一元配置の分散分析

分散分析

要因	自由度	平方和	平均平方	F値	p値(Prob>F)
肝嚢胞割合	3	1599.378	533.126	2.8939	0.0387*
誤差	107	19712.030	184.225		
全体(修正済み)	110	21311.408			

Liver specific QOL by % of liver cysts occupancy

肝嚢胞割合によるHepの一元配置分析



一元配置の分散分析

分散分析

要因	自由度	平方和	平均平方	F値	p値(Prob>F)
肝嚢胞割合	3	2832.890	944.297	9.4486	<.0001*
誤差	107	10693.601	99.940		
全体(修正済み)	110	13526.491			

HrQOL study of liver cysts

- **Specific HrQOL questionnaires reflects cysts volume occupancy.**
- **Burden of disease should be measured by specific HrQOL questionnaires.**
- **Development of kidney specific HrQOL questionnaires for ADPKD needed**