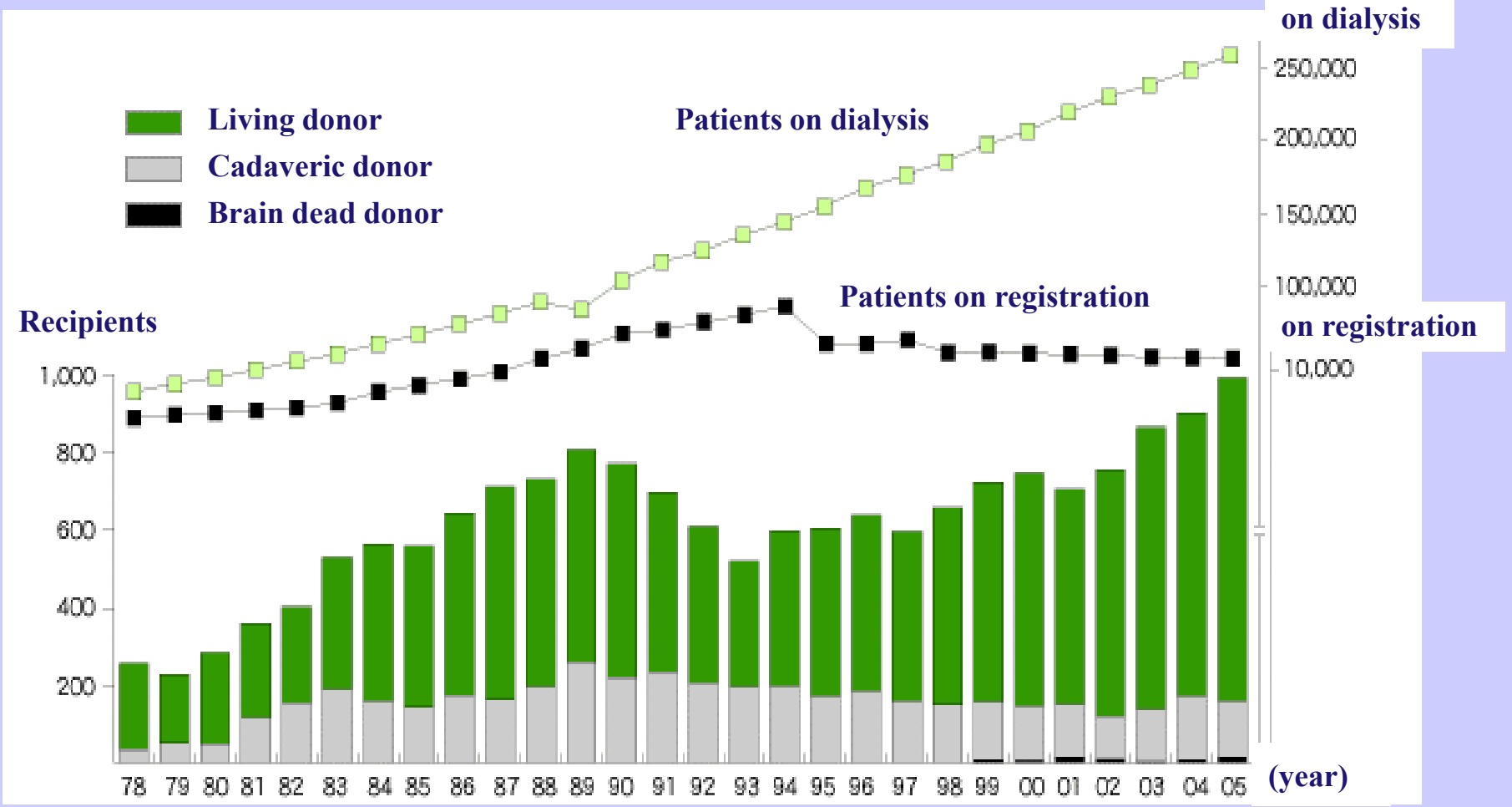
Historical consideration of ‘restored kidney’ transplantation, as of 2008

Yutaka Tsutsumi, M.D.,
Professor, Department of Pathology, Fujita Health University School of Medicine, Toyoake, Japan

Because of the grave shortage of deceased kidney allografts in Japan, ‘restored kidneys’ from living patients can be a new source of organs. From January 1991 through September 2006, 42 kidneys (8 benign pathology, 8 small renal cancers, 8 ureteral cancers, 6 aneurysms, 8 severe nephrotic syndrome from 4 patients and 4 ureteral stenosis) were obtained from 38 patients/donors after extensive discussion of treatment modalities and risks. All patients/donors agreed to undergo total nephrectomy. The lesions were removed/repaired *ex vivo* on the back table, then transplanted. All recipients were notified of all possible risks including donor disease recurrence. One, 5 and 10-year patient survival rates of restored transplant patients were 92.9%, 79.3% and 63.8%, respectively. One, 5 and 10-year graft survival rates of restored kidney transplant patients were 78.6%, 51.8% and 42.7%, respectively. There were no recurrences of renal cell carcinomas. There was one recurrence of ureteral cancer in the transplanted kidney 15 months after operation. In countries where deceased donors are scarce, such as Japan, the restored kidneys can be a last resort for renal allografts.

Ref.-1: Mannami M, et al. Last resort for renal transplant recipients, ‘restored kidneys’ from living donors/patients. Am J Transpl 2008; 8(4): 811-818. doi: 10.1111/j.1600-6143.2007.02145.x
Ref.-2: Ogawa Y, et al. Transplantation of restored kidneys from unrelated donors after resection of renal cell carcinoma: results from 10 patients. Transpl Proc 2015; 47(6): 1711-1719. doi: 10.1016/j.transproceed.2015.06.030

The numbers of patients on dialysis and on registration for renal transplantation and those received transplantation in Japan



Cadaveric renal transplantation in Japan（2006）

Patients on dialysis	**257,765**（2005. 12）
Patients on registration for renal transplantation	**11,564**（2006. 8）
Recipients of cadaveric kidney	**182**（2006）
Average waiting period	**16.6 years**

Living donor 939
Cadaver 182
Brain death 15 (in 2006)

My kidney（腎臓）is on sale: in Philippine

Reflecting serious shortage of organs in Japan

CAPD is NOT popular in Japan

Japan	**3.6%**
	(<10,000/260,000)
USA	14%
Canada	36%
UK	45%

CAPD can last only for 6.6 years on average.

CAPD is a tentative procedure until transplantation.

CAPD is cheeper than hemodialysis.

Most (more than 96%) of the Japanese renal failure patients are on hemodialysis.

“Restored Kidney”

The kidney from which the diseased portion has been removed or repaired

Examples of “restored kidney”

1. Kidney with renal artery aneurysm
2. Kidney with benign renal tumor
3. Kidney with small renal cell carcinoma
4. Kidney with cancer of the lower ureter
5. Kidney with ureteric stenosis
6. Kidney with intractable nephrotic syndrome

Nephrotic syndrome is usually secondary to systemic disorder

1. Minimal change nephrotic syndrome (caused by nephrosis-inducing factors in the plasma)
2. Immune complex-related glomerulopathy
3. Diabetic nephropathy
4. Amyloid nephropathy

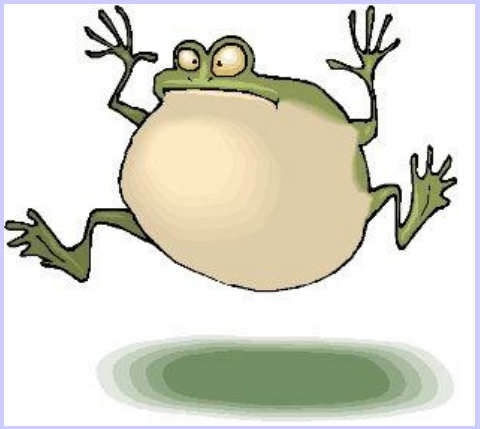
Marriam-Webster's dictionary

Definition of "normal"

not deviating from a norm, rule or principle
conforming to a type, standard or regular pattern

Definition of "abnormal"

deviating from the normal or average



Definition of "disease"

a condition of the living animal or plant body or of one of its parts that impairs normal functioning and is typically manifested by distinguishing signs and symptoms

Definition of “health” (WHO)

A dynamic state of complete physical, mental, spiritual and social well-being and not merely the absence of disease or infirmity

“Nobody is completely healthy”.
“Everybody is ill to some extent”.

Pathological basis of "restored kidney" transplantation

1) Disease usually occurs in a part of organs:
The residual part of the organ may be normal.

2) Disease with diffusely distributed impairment is usually caused by systemic disorders:
When transplanted into another healthy individual, the organ may function normally.

History of transplantation using "restored kidney" with non-neoplastic lesion in Japan

(up to the end of 2006: Mostly used for the family members, except for two cases)

Arteriovenous malformation	42 cases
Traumatic injury of renal vessel	5 cases
Reno-ureteric malformation/stenosis	11 cases
Aneurysm of renal artery	32 cases
Fibromuscular dysplasia of renal artery	5 cases
Total	**95 cases**

The first case of "restored kidney" transplantation in Japan: 1956

Donor: Idiopathic renal hemorrhage

Recipient: Acute renal failure due to mercury chloride intake (suicide)

1985: Arteriovenous malformation

3 cases (Toranomon Hospital, Tokyo)

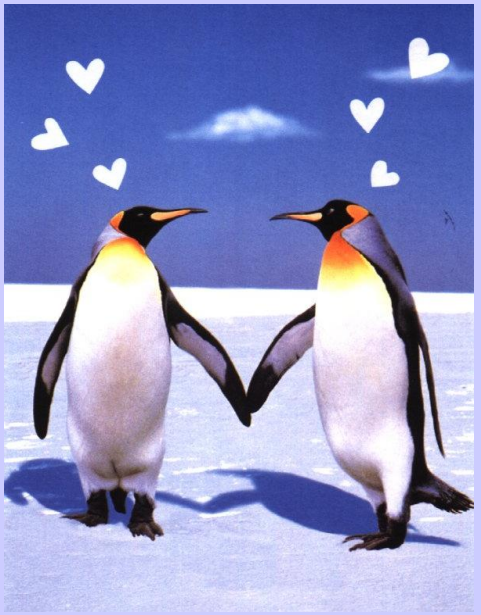
Arteriovenous malformation

1 case (Osaka University Hospital)

Aneurysm of renal artery

1 case (Sendai Social Insurance Hospital)

Large series of transplantation using “restored kidney” with non-neoplastic lesion in Japan



18 cases of arteriovenous malformation (1989)
Uwajima Municipal Hospital
8 cases of arteriovenous malformation (1990)
Hokkaido University Hospital
8 cases of aneurysm of renal artery (1998)
Tokyo Wemen’s Medical University Hospital

History of transplantation using "restored kidney" with nephrotic syndrome in Japan

<u>4 donors for 8 recipients</u>

3 cases (2000, 2000, 2003)
Uwajima Municipal Hospital
(including one case of lupus nephritis)
1 case (2004)
Uwajima Tokushukai Hospital
(minimal change)

Unique trial in Mannami's group

History of transplantation using “restored kidney” with benign neoplasm in Japan

(up to the end of 2006)

Angiomyolipoma

1998: Uwajima Municipal Hospital

2006: Uwajima Tokushukai Hospital

Other benign renal tumors

(removed under the diagnosis of renal cell carcinoma)

2000: Uwajima Municipal Hospital
(cavernous hemangioma)

2006: Uwajima Tokushukai Hospital (calcified cyst)

2006: Akita University Hospital (“benign tumor”)

History of transplantation using "restored kidney" with malignant neoplasm in Japan

(up to the end of 2006)

Ureteric carcinoma (8 cases)

Uwajima Municipal Hospital

5 cases: 1993, 1993, 1994, 1996, 2003

Kure Kyosai Hospital **3 cases**: 1997, 2001, 2001

Renal cell carcinoma (8 cases)

Uwajima Municipal Hospital

5 cases: 1996, 1999, 1999, 1999, 2001

Kure Kyosai Hospital **1 case**: 2001

Uwajima Tokushukai Hospital **2 cases**: 2006, 2006

Ureteric carcinoma recurred in one case (45 y-o male)

Case history

October, 1994: Restored kidney transplantation
(urothelial carcinoma G3 from a 65 y-o female)

January 1996: Recurrence in the renal pelvis
(locally removed)

January, 1997: Lung cancer with liver metastasis
(squamous cell carcinoma in sputum cytology)

January, 1999: Expired of hepatic coma

Rate of partial resection for small RCC in Japan

A total of 14 hospitals, including 4 universities, examined

(questionnaire study, 2004-2006)

All RCC surgical cases	941 cases
Partial resection cases	136 cases (**14.5%**)

T1a（tumor size: not more than 4.0 cm）286/593=**48.2%**

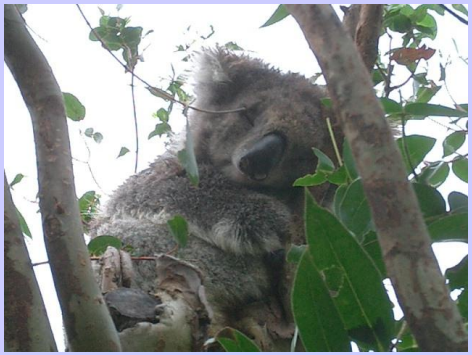
Partial resection of T1a cases (10 hospitals):

118/267 (mean: 44.2%), Range: 0-89.2%（**median**:**17.0%**）

Expected T1a cases for 14 hospitals: 941 x 0.482=454 cases

Expected rate of partial resection for 14 hospitals:

136/454＝30.0%（mean）; (**16.4%: median**）



The expected number of T1a RCC and ureteric cancer in Japan

Surgical cases of **RCC**, expectedly **6660 cases**

T1a lesions: 6660 x 0.482＝**3210 cases**

Nephrectomized T1a lesions:

3210 x 0.56＝1780 cases（based on the mean）

3210 x 0.83＝**2664 cases**（based on the median）

*30% of T1a cases provide **700 donor kidneys**.

Surgical cases of **ureteric cancer** : **2220 cases**

*10% of ureteric cancer cases provide **200 kidneys**.

Partial resection for small RCC. A yellow-colored small (25 mm)-sized RCC is located beneath the renal capsule. Partial nephrectomy is now common for the surgery of small RCC.

World history of transplantation using "restored kidney" with benign neoplasm

1990, France: **angiomyolipoma**
in cadaveric donor kidney

A total of 21 restored kidneys have been transplanted so far, including 4 Mannami cases.
(**angiomyolipoma** 15, others 6)

Note: Angiomyolipomas remaining in the transplant did not re-grow in three recipients. (1999, Germany, 1999. UK, 2006, Japan)

World history of transplantation using “restored kidney” with small renal cell carcinoma

1975: UK: 1 cm RCC (brain-dead case)
due to rejection, nephrectomy done 44 days later
1975: New York: 3 cm RCC (living sibling)
no recurrence for 8 years
1980: France:5 mm RCC removed 3 mo after transplantation
no recurrence for 9 years
1991: Poland: 4 mm RCC
the very first case of “restored” use
2001: Louisiana: 1 cm RCC (cadaver)

2004, Carrieri G (Foggia, Italy)

Review article in G. Ital. Nefrol (Italian)

Renal neoplasms and renal transplantation: Current problems and future perspectives

A proposal for the use of kidneys with subcapsular renal cell carcinoma less than 4 cm in size for transplantation

2005, Buell JF (Cinsinnati, Ohio)

analysis using database of the Israel Penn International Transplant Tumor Registry

Donor kidneys with small renal cell cancers: Can they be transplanted? *Transplant Proc* 37: 581-582

14 donor kidneys with small renal cell carcinoma (11 living donors and 3 cadaveric donors) were used for transplantation after restoration (tumor size: 0.5-4 cm)

Results: No recurrence recorded (mean follow-up period 69 months, with a range of 14 to 200 months)

Conclusion: The use of organs from donors with small, localized renal cell carcinoma is acceptable.

Comments: He experienced two such cases (living donors) by himself during past 3 years.

Recent papers on “restored kidney” transplantation

2007, Nicol HD (Brisbane, Australia)
49 cases of restored kidney transplantation
2007, Mitsuhata N (Kure Kyosai Hospital): 2 cases
2007, Whitson J (San Francisco, California): 1 case
2008, Mannami M (Uwajima Tokushukai Hospital)
8 cases (including Mitsuhata’s cases)

*A total of **78** restored kidney transplantation cases with small renal cell carcinoma recorded.*

No recurrence seen!

Thank you very much for your attention