移植施設毎の症例一覧表





各施設の症例を示し、 各々の症例の登録状 況がわかる。

登録の完了したもの、 追跡データを入力すべ きもの、などが表示され ている。

症例の詳細を入力する画面







LITRE-Jのメリット

- 何時でも、何処でも入力可能
- 自動的にスコアー入力
- 入力ミスの減少(入力チェック機能)
- コンピュータの種類に依存しない→ Windowsでも、Macでも可
- 何時でも、システムのversion up が可能

厚生労働科学研究費補助金



平成20~22年度

一般公募型

腎臓移植の成績向上をめざした臨床データ解析を目的とした症例登録と追跡制度の確立並びにドナー及びレシピエントの安全性確保とQOL向上に関する研究

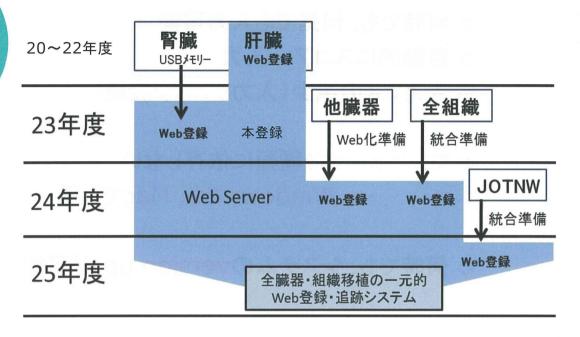
平成23~25年度

指定型

全ての臓器と組織移植症例の一元的な登録と追跡制度の確立ならびにドナーとレシピエントの安全性確保とQOL向上に関する研究

全ての臓器と組織移植症例の一元的な登録と追跡制度の確立ならびにドナーとレシピエントの安全性確保とQOL向上に関する研究

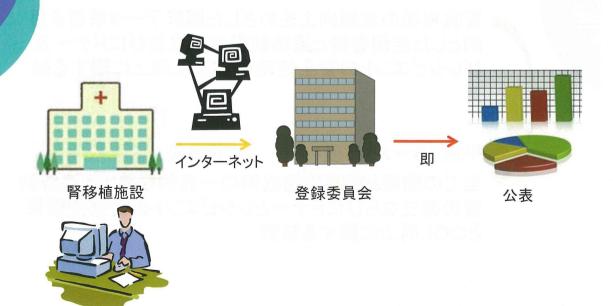




JARTRE-W system

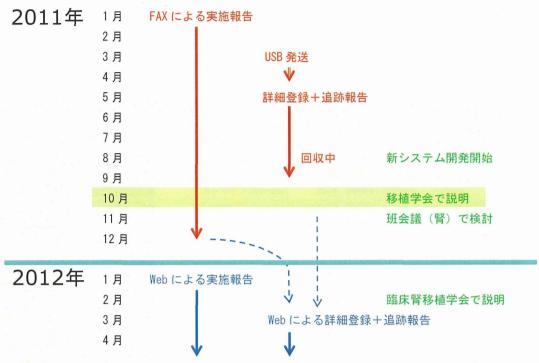


○ 2012年1月1日からの登録は完全にweb化









JARTRE-W ログイン画面

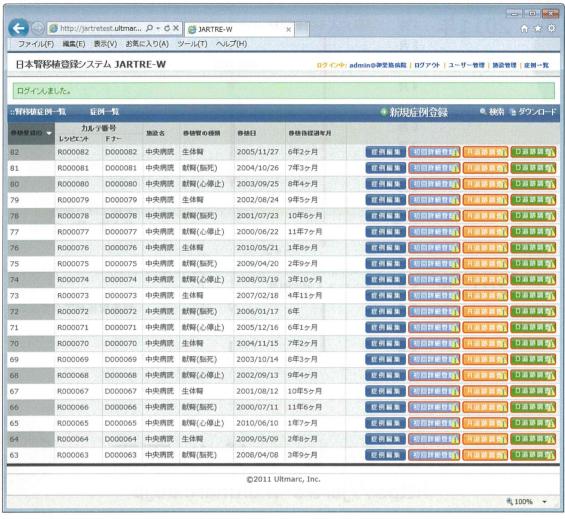


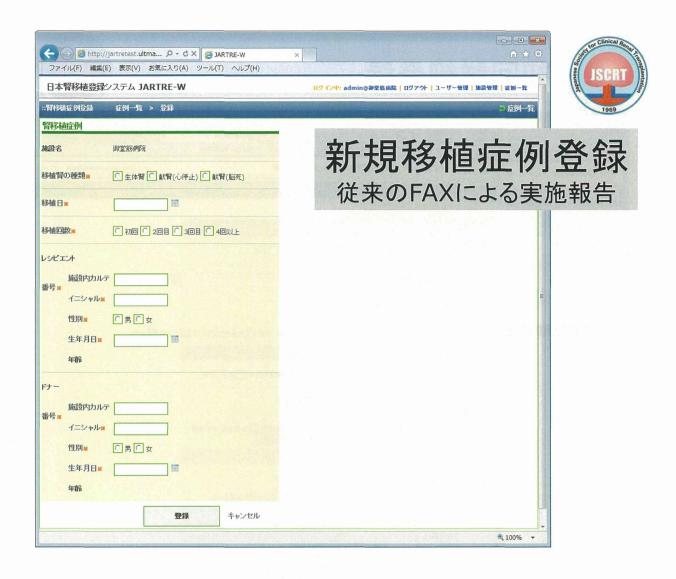
https://jartre-w.ultmarc.co.jp





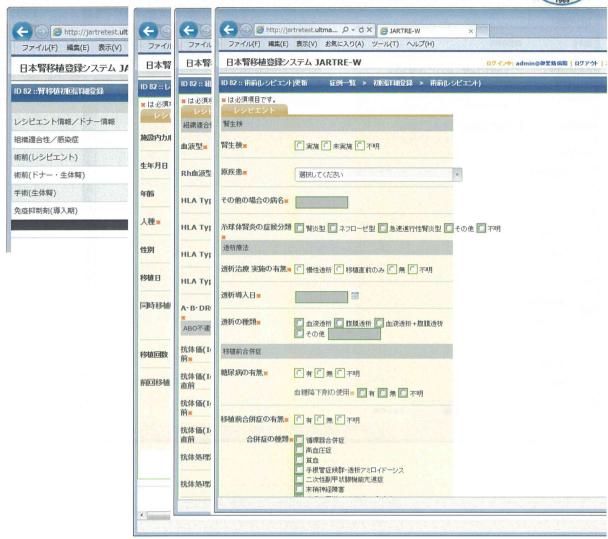
症例一覧画面





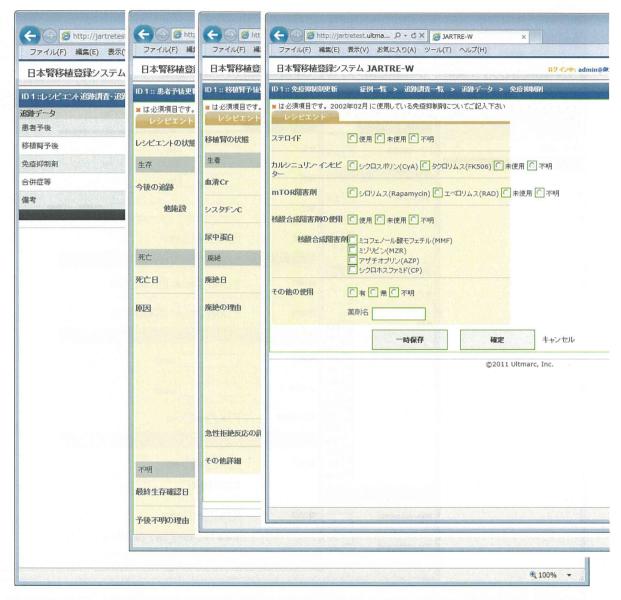
初回詳細登録







レシピエント追跡調査





ドナー追跡調査

D1::ドナー高級調査・選挙データ 2002年02月 2002年02月	← ② ● http://jartretest.ultma ファイル(F) 編集(E) 表示(V) お気	(http://	E) 表示(V	ファイル(F) 編	tp://jartretest.ultma クィ & X () jartretest.ultma クィ は X () jartretest.ultma カ は X () jartret) ヘルプ(H)	
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				喫煙歷	○ 有 ○ 無 ○ 不明		
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原因				精神的	○良好○変化無し○不良○	不明	
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新システムまでのロードマップ





すでに新しい腎移植登録が可能



- 現在、マニュアルの作成中。
- 今後、腎移植施設の登録、登録担当者の登録、 パス ワードの配布。
- 必要なら、各施設の倫理委員会でインターネット 登録について申請し、認可を得る。
- ----> 2012年1月1日~ FAXでの実施報告 なし 直接、インターネットで登録

ISURT ISURT ISON

日本移植学会倫理委員会の見解

- 1. 登録に関する個別同意書の取得は不要で、口頭や掲示で の「もし登録に承諾頂けない場合には、担当医や窓口まで お申し出下さい」といった表現で良い。
- 2. その際、登録システムを明示する必要はなく、「登録内容は個人が特定できないような形にして、プライバシーには最細の注意をして、学術目的のために学会などが運営する登録制度に利用させて頂きます」でも良いし、「肝移植研究会の登録制度」と明示しても良い。
- 3. 治療介入がないので、各施設のIRB申請は不要と判断していますが、これに関しては各施設の判断が優先される。

今後の予定



- 移植施設の登録担当者へ、IDとパスワードをマニュアルとともに郵送
- 初回ログインの時に、メールアドレスを登録し、以後、2012年1月1日からの症例を登録
- 2011年の症例の詳細登録、2010年以前の症例 の追跡調査は、2~3ヶ月後から可能
- 必要なら、各施設の倫理委員会でインターネット登録について申請し、認可を得る。

Multistate time-to-event modelling for kidney transplantation registry data



Makiko Naka Mieno*1, Takashi Yaqisawa*2, Kenji Yuzawa*3, Shiro Takahara*4

- 1. Department of Medical Informatics, Jichi Medical University, *2. Department of Urology, Jichi Medical University, *3. Department of Transplantation Surgery, National Hospital Organization Mito Medical Center,
 - *4. Department of Advanced Technology of Transplantation, Osaka University Graduate School of Medicine

INTRODUCTION

- •In the event history data analysis, multistate time-to-event modelling approach has been widely used. For kidney transplantation data, death with functioning graft is a common cause of graft loss.
- •The differences of the risk factors onto these competing events, death with functioning graft and other graft failure, have not been examined in detail

AIMS

To evaluate the long-term graft survival with competing risks

and the effect of the covariates on the cumulative incidence of graft failure or death with functioning graft.

SUBJECTS

- National registry database for kidney transplantation in Japan.
- •All transplant cases performed in Japan are to be registered. The database is updated every year.
- Baseline characteristics: transplantation date, centre, living / deceased (heart-beating or nonheart beating) donor information, recipient's and donor's sex, age, race and blood types (HLA and ABO), original diseases, ischemia time, pretransplant complications, duration of dialysis therapy, the status of viral antigens and antibodies, immunosupressants used, etc.
- •Follow-up information: recipient's survival and graft survival, cause of death, cause of nonfunction, complications, and acute rejection history, as well as donor's survival, renal function for living donor transplants.
- ■We analysed first-time 10,517 living donor transplants and 2,792 deceased donor transplants performed between 1992 and 2009. The median follow-up period was 6 years.
- ●General Kaplan-Meier estimates for 1-year, 5year graft survival were 96.2%, 89.0% (living donor transplants) and 87.7%, 73.8% (deceased donor transplants), respectively.
- •There were 2,751 graft failures, including 592 death with functioning graft cases.

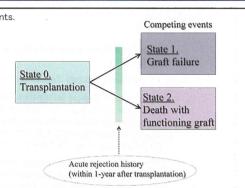
MODELS

Multistate time-to-event model with competing events

- Fine & Gray's proportional hazards model was used to estimate the covariate effects.
- recipient's sex, age, donor's age, the number of HLA-mismatches, pre-transplant dialysis, primary cause of end-stage renal disease (diabetes or not), the year of the transplantation performed, and the warm and cold ischemia time (only for the deceased donor transplants).
- The subdistribution hazard function for cause k is:

$$h_k^*(t;z) = h_{0k}^*(t) \exp(\beta Z)$$

which enables the direct estimation of the effect of covariates



RESULTS

Table 1a. Hazard ratios for graft failure without death (living)

Variables	Hazard ratio [95%CI]	P-value
Year of transplantation	0.92 [0.90-0.94]	<.0001
Recipient's sex (F/M)	0.77 [0.66-0.89]	0.0004
Recipient's age (/10)	0.93 [0.88-0.99]	0.028
Donor's age (/10)	1.28 [1.20-1.38]	<.0001
No. of HLA-mismatch	1.09 [1.02-1.15]	0.009
Pre-transplant dialysis (year)	0.98 [0.83-1.16]	0.810
Original disease (DM/not DM)	1.74 [1.32-2.30]	<.0001

Table 2a. Hazard ratios for graft failure without death (deceased)

Variables	Hazard ratio [95%CI]	P-value	
Year of transplantation	0.95 [0.92-0.97]	<.0001	
Recipient's sex (F/M)	0.77 [0.62-0.97]	0.025	
Recipient's age (/10)	1.00 [0.90-1.10]	0.948	
Donor's age (/10)	1.17 [1.09-1.26]	<.0001	
No. of HLA-mismatch	1.08 [0.99-1.18]	0.065	
Pre-transplant dialysis (year)	0.99 [0.89-1.12]	0.936	
Warm ischemia time (min)	1.22 [1.04-1.43]	0.017	
Cold ischemia time (hour)	1.09 [0.95-1.25]	0.203	
Original disease (DM/not DM)	1.25 [0.71-2.20]	0.443	

Table 1b. Hazard ratios for death with functioning (living)

		-,
Variables	Hazard ratio [95%CI]	P-value
Year of transplantation	0.91 [0.89-0.94]	<.0001
Recipient's sex (F/M)	0.78 [0.59-1.04]	0.094
Recipient's age (/10)	1.68 [1.51-1.88]	<.0001
Donor's age (/10)	1.03 [0.92-1.17]	0.569
No. of HLA-mismatch	0.99 [0.90-1.09]	0.800
Pre-transplant dialysis (year)	1.48 [1.12-1.96]	0.006
Original disease (DM/not DM)	1.23 [0.78-1.94]	0.369

Table 2b. Hazard ratios for death with functioning (deceased)

Variables	Hazard ratio [95%CI]	P-value
Year of transplantation	0.94 [0.90-0.98]	0.007
Recipient's sex (F/M)	0.44 [0.29-0.67]	0.0001
Recipient's age (/10)	1.64 [1.34-2.02]	<.0001
Donor's age (/10)	1.07 [0.99-1.02]	0.225
No. of HLA-mismatch	1.06 [0.93-1.22]	0.382
Pre-transplant dialysis (year)	1.34 [1.10-1.62]	0.004
Warm ischemia time (min)	1.13 [0.86-1.48]	0.390
Cold ischemia time (hour)	1.17 [0.93-1.46]	0.174
Original disease (DM/not DM)	2.20 [0.99-4.88]	0.052

- For graft failure without death: donor's factor, histocompatibility, and ischemia time were more critical
- •For death with functioning: recipient's factors were more influential.

CONCLUSIONS

- When estimating the graft survival, causes of graft loss should be considered
- Multistate time-to-event modelling approach illustrates the situation well
- Further study is needed for modelling to include the intermediate state information more appropriately.

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Fine J. and Gray R. A proportional hazards model for subdistribution of a competing risk. Journal of the American Statistical Association 1999.

Kalbfleisch JD. and Prentice RL. The Statistical Analysis of Failure Time Data 2nd Edition. Wiley, 2002.

Pintilie M. Competing Risks - A Practical Perspective. Wiley,

Opelz G and Döhler B. Association of HLA mismatch with death with a functioning graft after kidney transplantation: a ollaborative transplant study report. Am J Transplant 2012.

^{*} This work was supported by Health and Labour Sciences Research Grant in Japan.

pupae as there was in the Neural Network Method that, especially in its capacity to emulate non-linear data, seems to be an interesting option.

P2K02

Multistate time-to-event modelling for kidney transplantation registry data

Makiko Mieno, Takashi Yagisawa, Kenji Yuzawa, Shiro Takahara

Department of Medical Informatics, Jichi Medical University; Department of Urology, Jichi Medical University; Department of Transplantation Surgery, National Hospital Organization Mito Medical Center; Department of Advanced Technology of Transplantation, Osaka University Graduate School of Medicine

Background In the event history data analysis, multistate time-toevent modelling approach has been widely used. For kidney transplantation data, death with functioning graft is a common cause of graft loss. The differences of the risk factors onto these competing events, death with functioning graft and other graft failure, have not been examined in detail.

Objectives To evaluate the long-term graft survival with competing risks, and the effect of the covariates on the cumulative incidence of graft failure or death with functioning graft.

Methods By using the kidney transplantation registry data in Japan from 1992 to 2009, we analysed first-time 10,517 living donor transplants and 2,792 deceased donor transplants. The association of the covariates with the outcomes was evaluated using the restricted cubic splines, and the multivariate analyses, the use of Fine and Gray proportional hazards model for the subdistribution of the competing risks. The recipient's sex, recipient's age, donor's age, the number of HLA-mismatches, pre-transplant dialysis, primary cause of end-stage renal disease (diabetes or not) and the year of the transplantation performed were examined for living donor transplants. The warm ischemia time and the total ischemia time were also included for deceased donor transplants analysis. Additionally, the acute rejection history within 1-year after transplantation was considered as the intermediate state.

Results The hazard ratios of the transplantation year showed significantly decreasing trend for graft failure and death with functioning graft. For graft failure event, male recipient and older donor were significant risk factors whereas older recipient and longer pre-transplant dialysis duration were more important factors for death with functioning graft event. The acute rejection state in the event history was also nonignorable for the future risks of the events.

Conclusions When calculating graft survival, causes of graft loss should be considered and multistate modelling approach illustrates the situation well.

P2K03

Longitudinal discrete data analysis: comparison of four statistical models applied on repeated malaria episodes data from Mali

Sagara Issaka, Dicko Alassane, Djimde Abdoulaye, Doumbo Ogobara K, Giorgi Roch, Gaudart Jean

Université des Sciences, Techniques et Technologies; Aix-Marseille Univ, UMR912 (SESSTIM), 13005 Marseille, France

Background The analysis of repetitive events data in cohort studies is quite common in biomedicine. The literature review indicates that statistical models used in analyzing these data are often based on time to the first event or consider events within subject as independent,

therefore ignoring the non-independence of events in the same individual. However, methods exist to analyze data taking into account the non-independence of repeated events within subjects.

Objectives This work aimed to analyze repeated malaria episodes with different models in order to advise on the best model estimating malaria risk in respective to covariates.

Methods Data were collected from July 2005 to July 2007 in Bougala-Hameau, Sikasso, Mali. The study main objective was to compare malaria incidences in 3 different artemisinin based combination therapy (ACT) arms: artesunate/amodiaquine (AS + AQ), artesunate/sulfadoxine-pyrimethamine (AS + SP) and artemether-lumefantrine (AL). The AL arm and the age group ≥15 years old were used as reference groups in RR computing. We used 4 different models to analyze the data using Stata[®]: the Poisson model, the generalized estimating equation (GEE) using Poisson distribution, the extended Cox models (Anderson-Gill model -AG-) and the frailty model. Model comparison was based on the magnitude and confidence intervals of relative risks (RR) in respective to relevant covariates, power and goodness-of-fit criteria.

Results The 780 subjects enrolled yield a total of 2,473 malaria episodes. The malaria episode RR for patients in the AS + AQ and AS + SP arms were respectively: 0.85 (0.77–0.93) and 0.82 (0.74–0.90) using Poisson model, 0.95 (0.84–1.08) and 0.90 (0.80–1.03) using the *GEE model*, 0.78 (0.65–0.92) 0.79 (0.66–0.94) using Anderson-Gill model, 0.61 (0.45–0.84) and 0.64 (0.47–0.88) using Frailty model. The malaria episodes RR for the patients in the age groups; 10–14 years old, 5–9 years old and <5 years were respectively: 1.60 (1.11–2.30), 2.40 (1.75–3.30) and 2.71 (1.98–3.71) using Poisson model, 1.68 (0.90–3.14), 2.15 (1.22–3.79) and 2.28 (1.30–4.0) using the *GEE model*, 1.69 (0.81–3.56), 3.22 (1.68–6.17) and 3.60 (1.89–6.84) using Anderson-Gill model, 2.47 (0.75–8.12), 7.51 (2.64–21.34) and 9.11 (3.25–25.57) using Frailty model.

Conclusion All models (except GEE for one covariate) although different in magnitude were able to detect the significant covariate effects showing the power of these models. Anderson-Gill and Frailty models estimated RR with higher magnitude and wider precision.

P2K04

Optimal control applied to tuberculosis models

Cristiana Silva, Delfim Torres

CIDMA, Department of Mathematics, University of Aveiro

Background Most cases of tuberculosis (TB) are caused by the Mycobacterium tuberculosis, which is usually transmitted via airborne infection from someone who has active TB. Approximately 10 % of infected people with Mycobacterium tuberculosis develop active TB disease, that is, approximately 90 % of infected people remain latent. Latent infected TB people are asymptomatic and do not transmit TB, but may progress to active TB through endogenous reactivation or exogenous reinfection. The anti-TB drugs developed since 1940 have helped to reduce the mortality rates significantly: in clinical cases, cure rates of 90 % have been documented. However, TB remains a global public health emergency and following the World Health Organization (WHO) in 2010, there were an estimated 8.5–9.2 million cases and 1.2–1.5 million deaths (including deaths from TB among HIV-positive people). TB is the second leading cause of death from an infectious disease worldwide (after HIV).

Optimal control is a branch of mathematics that involves finding optimal ways of controlling a dynamic system. While the usefulness of optimal control theory in epidemiology is nowadays well recognized, results pertaining to tuberculosis are a rarity [1].

Objective and methods We apply optimal control theory to a TB model given by a system of ordinary differential equations. There are



Online Registry and Tracking System for **Kidney and Liver Transplantation in Japan**









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 Dept. of Surg., Osaka Univ. Grad. School of Med.
 Dept. of Med. Informatics, Center of Information, Jichi Med. Univ.
- 4, Dept. of Advanced Technology of Transpl., Osaka Univ. Grad. School of Med.

Japan

TTS2012 Berlin, July 15, 2012

Introduction

Following to The Declaration of Istanbul 2008, the registration committees of Japanese Society for Clinical Renal Transplantation and Japanese Liver Transplantation Society, supervised by Japan Society for Transplantation, had planned to establish new registry and tracking systems for kidney and liver transplantation on recipients and donors.

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1

Evolution in Registration System for Organ Transplantation in Japan

1st Paper Registration~2007

2nd Electrical Registration

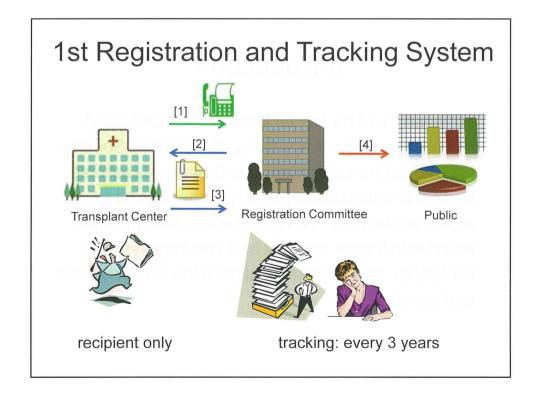
using USB memory

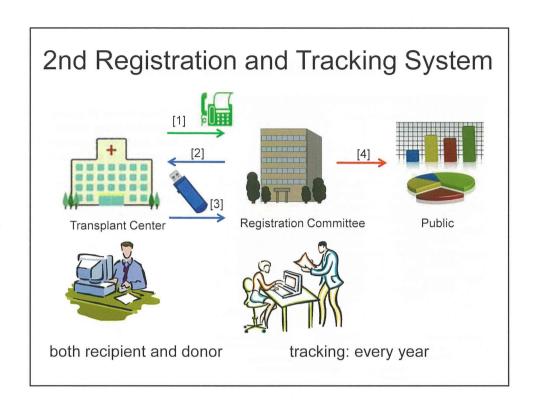
2008~2011 in renal Tx

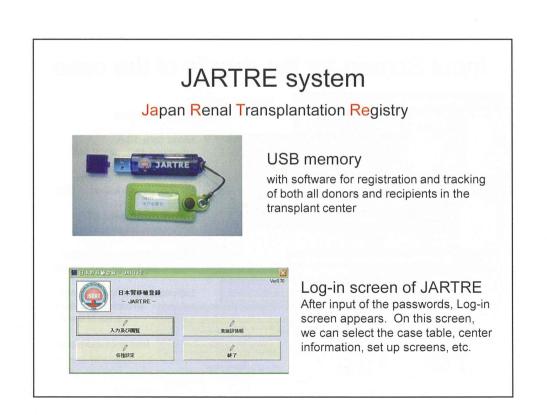
• 3rd Internet Registration

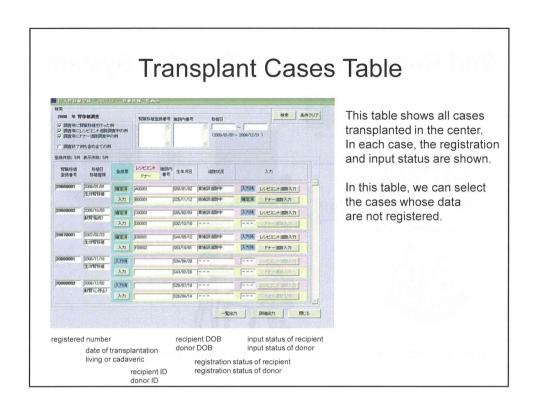
2011~ in Liver Tx

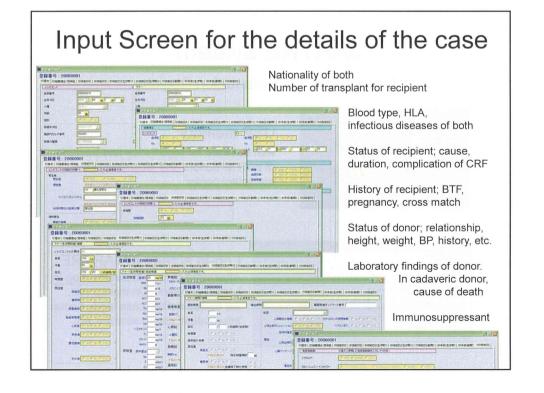
2012~ in Renal Tx

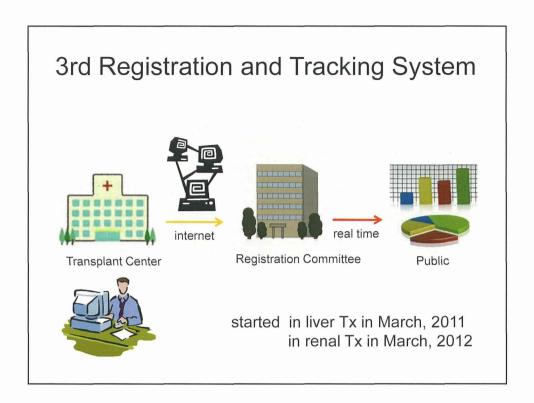


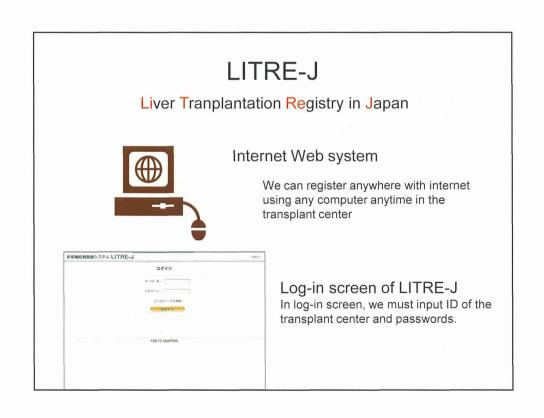












Transplant Cases Table



This table shows all cases transplanted in the center. In each case, the registration and input status are shown.

In this table, we can select the cases whose data are not registered.

