LUNG TRANSPLANTATION

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Content

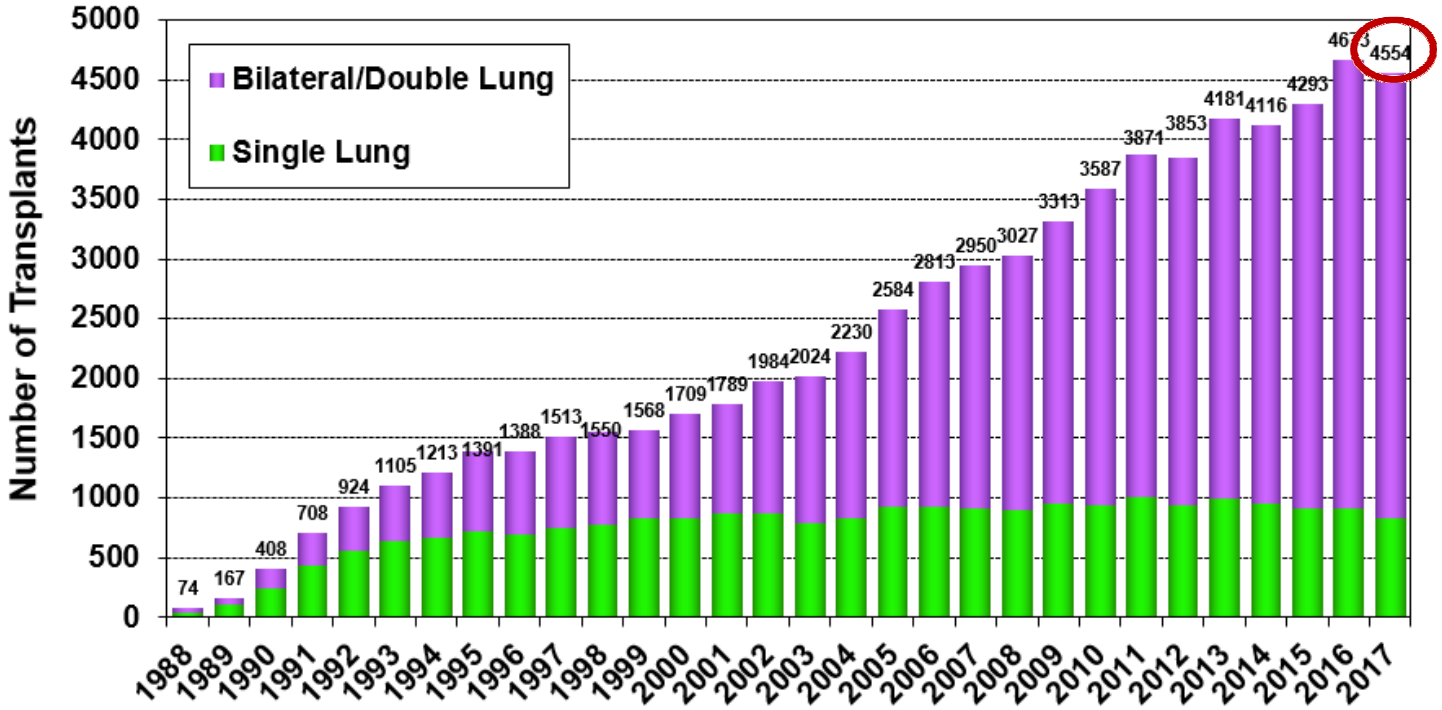
SNUH 분당서울대학교병원

Histologic aspect

- In 1947, Vladimir Demikhove performed the first lung transplant in a dog.
- Dr. James D. Hardy and colleagues performed the **first human** lung transplant in **1963.** [left lung TPL, 18days survive]
- The first successful human lung transplant was done in **1986** by the Toronto Lung Transplant Group. [Dr. Joel Cooper]
- In 1988, Dr. Alexander Patterson described the technique of double lung transplantation.
- Dr. Denton Cooley and associates were the first to attempt heart-lung transplantation in 1968.
- Since then, more than 15,000 lung transplants have been done.

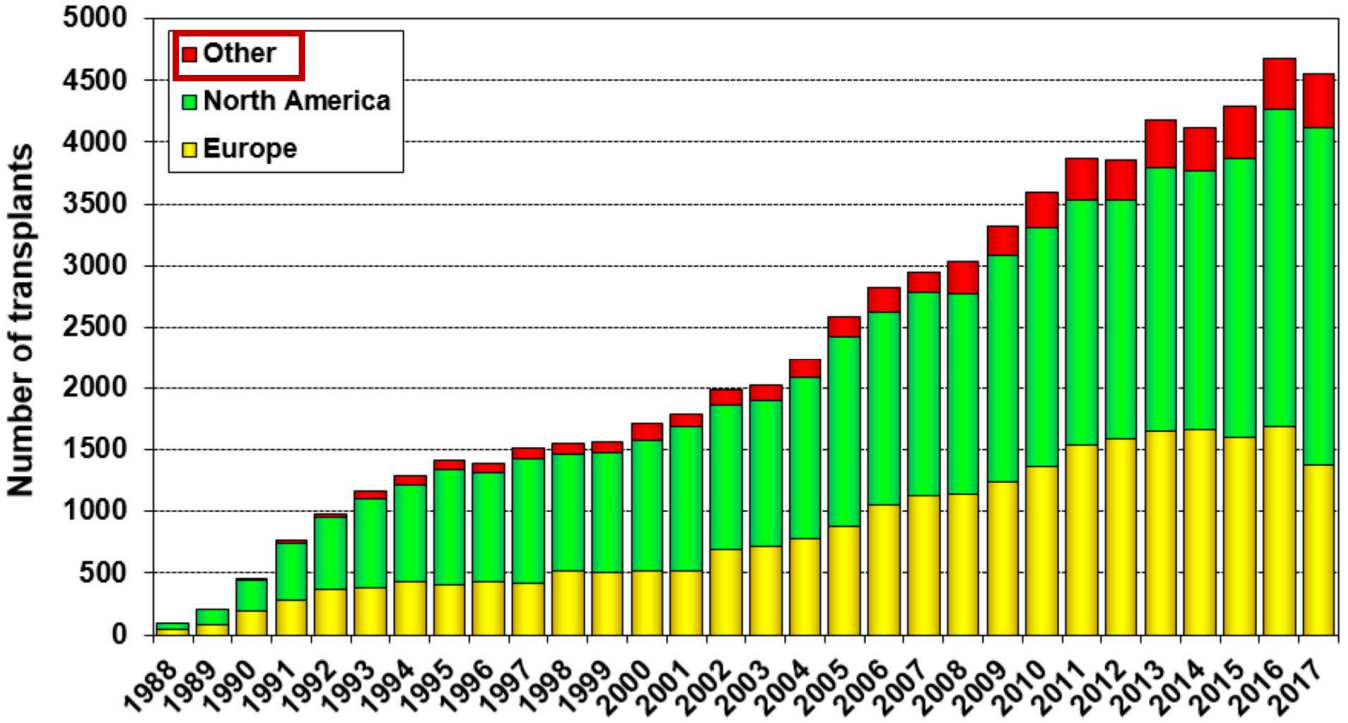
1 Lung Transplantation

Overall Lung Transplantation Statistics 2019



1 Lung Transplantation

Overall Lung Transplantation Statistics 2019



When to consider transplant

- **General selection criteria**
  1. Clinically and physiologically severe lung disease
  2. Medical therapy ineffective or unavailable
  3. Substantial limitations in activities of daily living
  4. Limited life expectancy
  5. Adequate cardiac function without significant coronary disease
  6. Ambulatory, with rehabilitation potential
  7. Acceptable nutritional status
  8. Satisfactory psychosocial profile and emotional support system

TRANSPLANTATION *:35(7);365-370*

Absolute contraindications

- Extra-pulmonic disease
- HIV Infection
- Malignancy with in prior 2yrs
- Hepatitis B antigen positivity
- Hepatitis c biopsy proven liver disease
- Severe musculoskeletal disease
- Substance addiction in prior 6months
- Absence of reliable support system
- Untreated psychosocial problems
- Non-compliance

TRANSPLANTATION *:35(7);365-370*

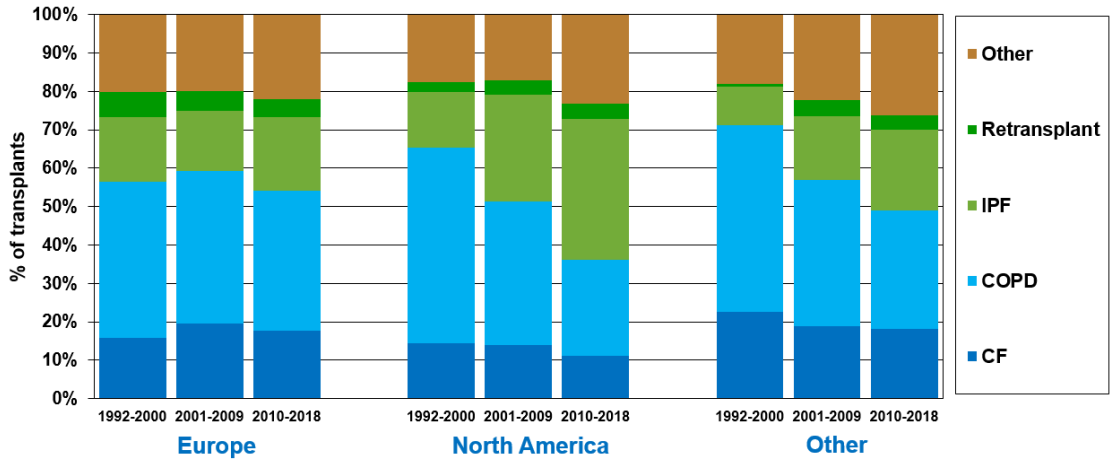
Relative contraindications

- Age > 65
- Critical or unstable medical condition
- Systemic or multisystem extrapulmonic disease
- Pan resistant organisms
- Symptomatic osteoporosis
- Mechanical ventilation
- BMI < 17 or > 30

TRANSPLANTATION *:35(7);365-370*

Lung Transplantation

Overall Lung Transplantation Statistics 2021



❖ Indication of lung transplantation

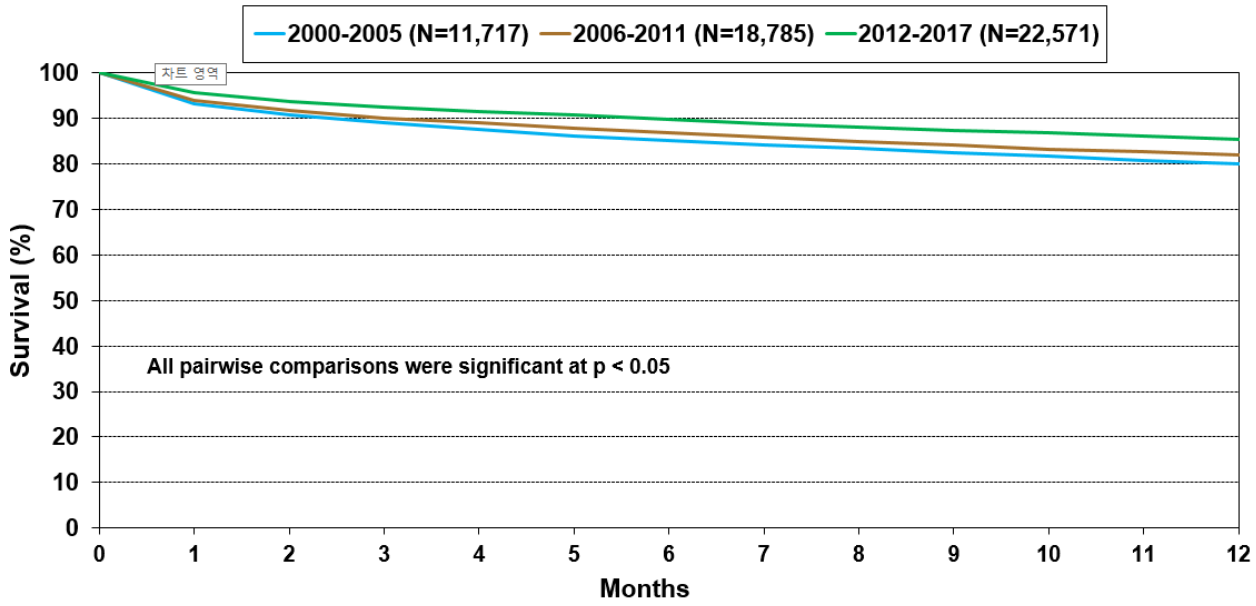
1. Obstructive lung disease
   COPD
2. Restrictive lung disease
   IPF
   ILD
3. Septic lung disease
   CF
   Bilateral bronchiectasis
4. Pulmonary vascular disease
   Primary pulmonary hypertension
   Eisenmenger's syndrome

Survival of Lung Transplantation Statistics 2021

Adult Lung Transplants

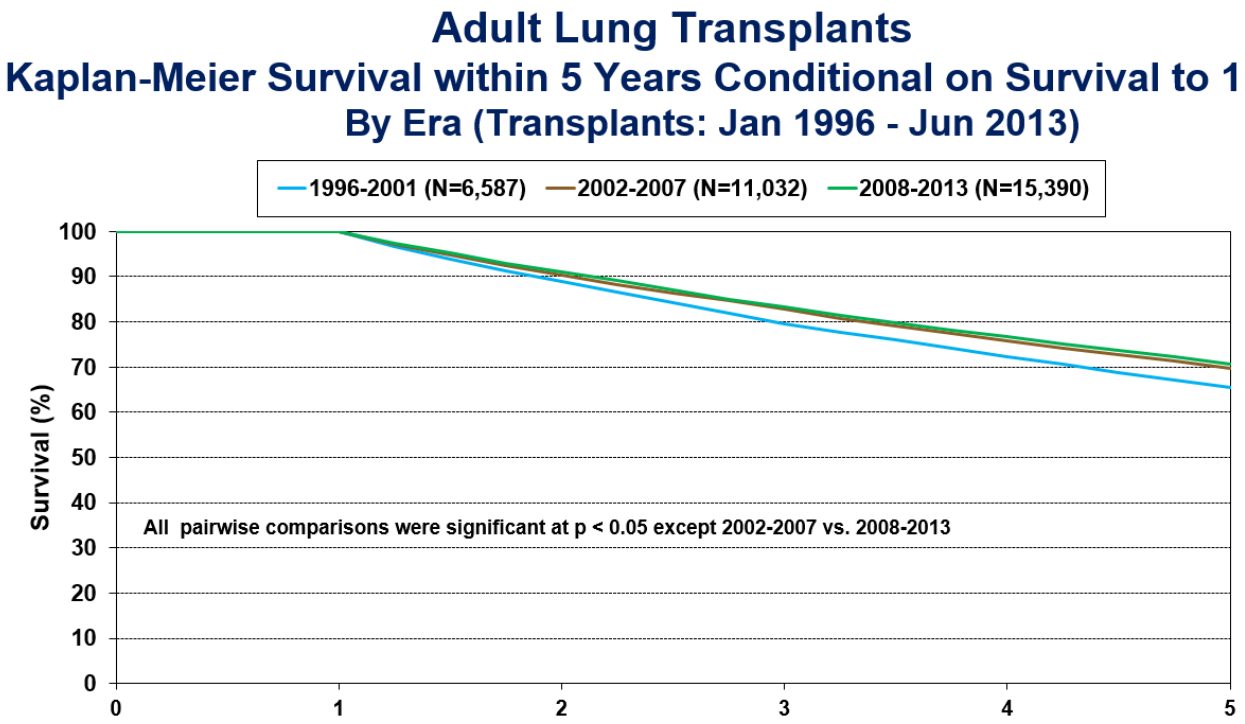
Kaplan-Meier Survival within 12 Months by Era

(Transplants: Jan 2000 – Jun 2017)



1yr survival : 85%

Survival of Lung Transplantation Statistics 2021

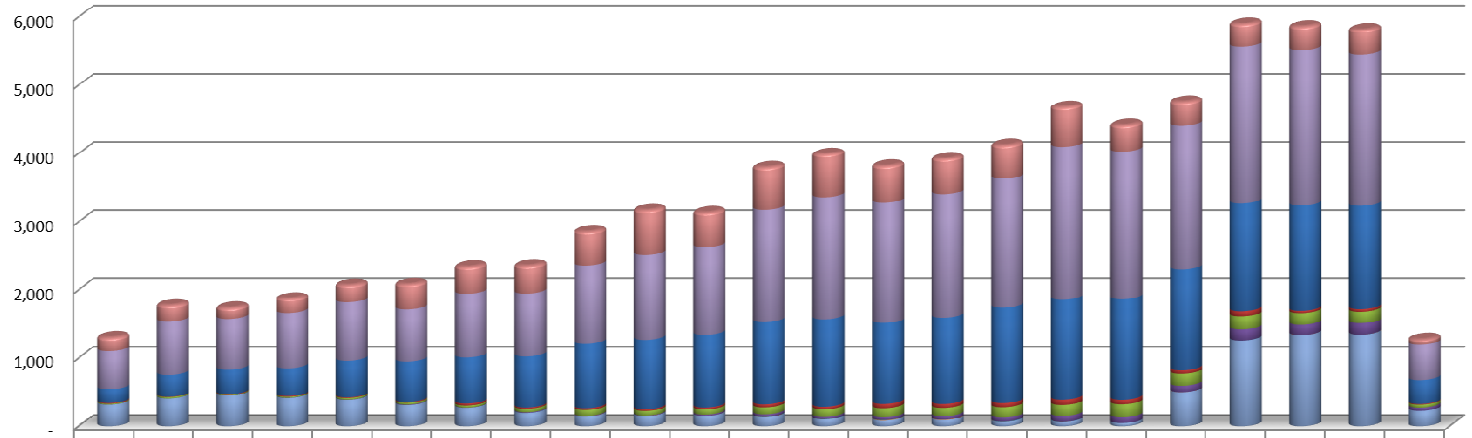


5yr survival : 70%

1 Lung Transplantation

KONOS, 2022, 1분기 통계

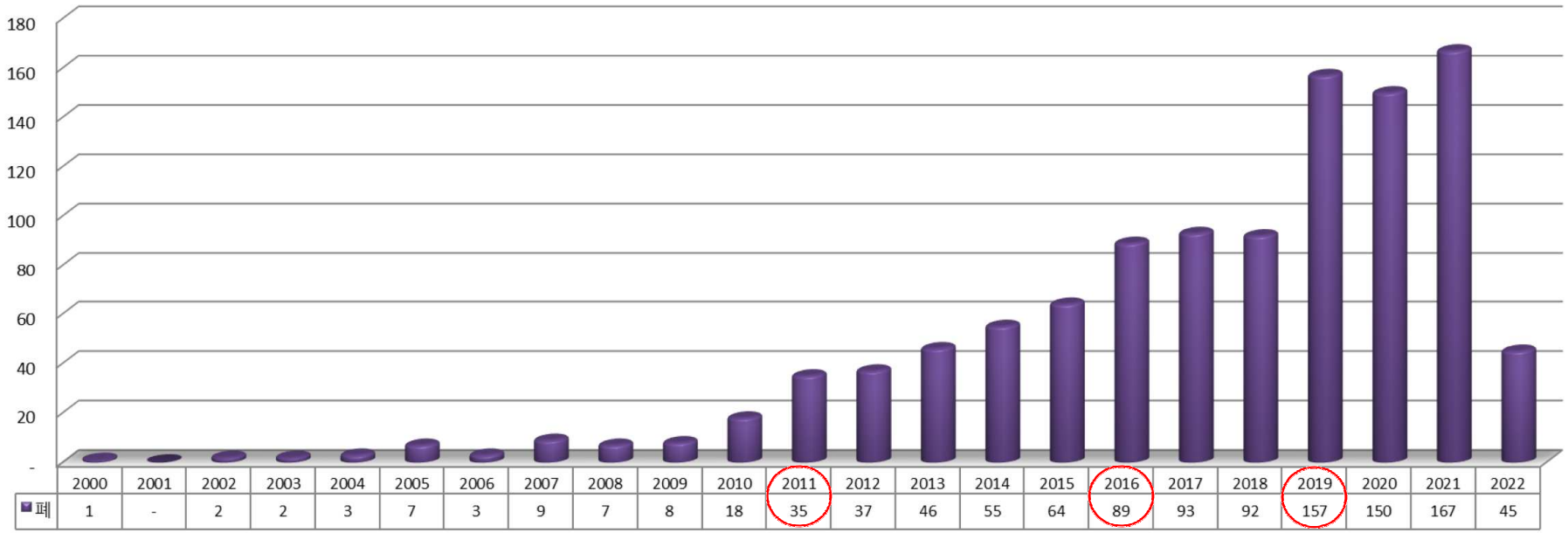
장기별 전체 장기이식 현황



	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
췌장	204	233	160	212	255	368	397	409	496	662	505	626	632	543	522	492	587	390	349	334	347	363	73
신장	554	788	741	808	851	760	935	924	1,142	1,238	1,280	1,639	1,788	1,762	1,809	1,892	2,236	2,164	2,108	2,299	2,281	2,225	528
간장	205	323	364	414	544	508	678	749	950	1,019	1,066	1,213	1,286	1,188	1,267	1,400	1,473	1,482	1,476	1,580	1,543	1,514	350
췌상	11	5	8	12	10	12	29	18	24	23	27	43	36	61	55	59	74	63	58	75	82	87	10
심장	12	21	11	15	23	26	29	50	84	65	73	98	107	127	118	145	156	184	176	194	173	168	43
폐	1	-	2	2	3	7	3	9	7	8	18	35	37	46	55	64	89	93	92	157	150	167	45
췌도	-	-	-	-	-	-	-	1	-	-	-	3	3	3	-	4	2	1	-	1	-	1	-
소장	-	-	-	-	-	-	-	-	2	1	1	2	1	5	5	1	1	-	1	-	1	1	-
조혈모	318	405	452	413	386	312	273	199	150	155	158	141	103	86	94	67	66	45	502	1,762	1,338	1,344	230

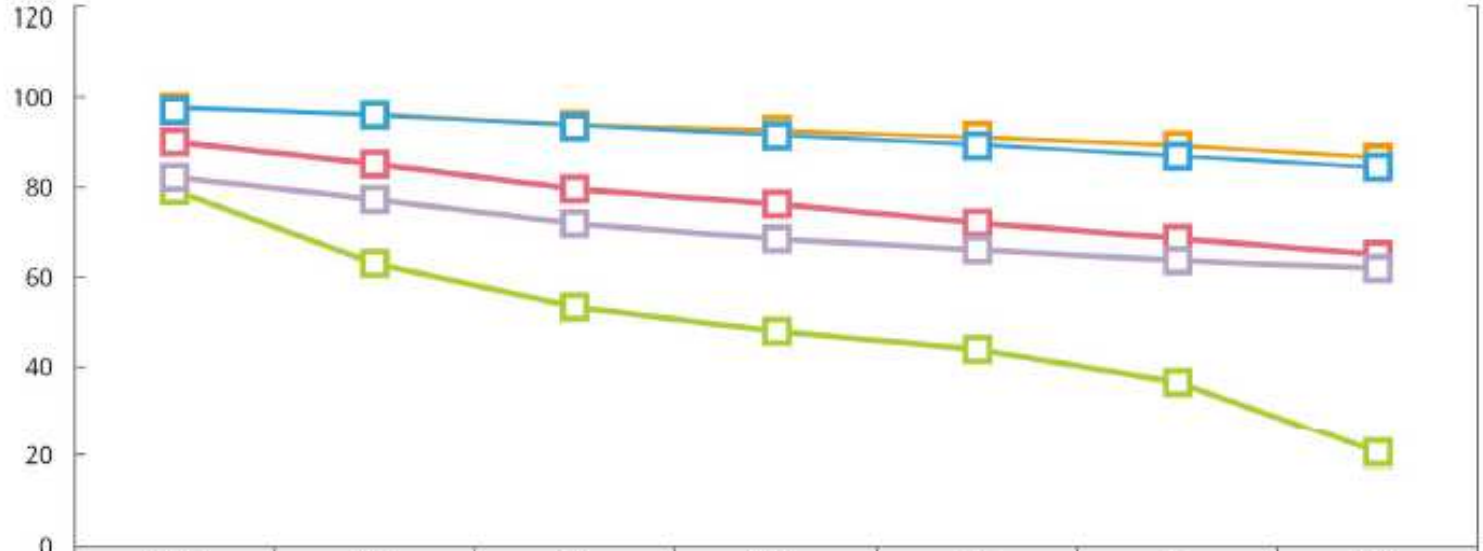
1 Lung Transplantation

LUNG TPL IN KOREA



	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
폐	1	-	2	2	3	7	3	9	7	8	18	35	37	46	55	64	89	93	92	157	150	167	45

2 Lung Transplantation



	3개월	1년	3년	5년	7년	9년	11년
신장	97.61	96.04	93.77	91.58	89.49	86.95	84.41
간장	82.24	77.31	71.89	68.46	66.04	63.68	61.92
췌장	97.79	96.24	93.90	92.56	91.04	89.31	86.59
심장	90.08	85.21	79.60	76.26	72.06	68.59	64.97
폐	79.30	62.99	53.37	47.90	43.92	36.58	20.63

1 Lung Transplantation

구분	2015	2016	2017	2018	2019
계	64	89	93	92	157
Asbestosis		1		1	
Bronchiectasis	4	4	4	1	9
Cystic Fibrosis				1	2
Eisenmenger Syndrome		1			1
Emphysema		3		1	4
Idiopathic Pulmonary Fibrosis	30	44	48	41	75
Lymphangioleiomyomatosis		1	1	1	1
Primary Pulmonary Hypertension	2	3	4	3	2
이식후 Brinchiolitis Obliterance	6	3	7	4	10
기타	22	29	29	39	53

2 Donor lung procurement

평균 대기 시간 ; 4-6개월

구분	2015	2016	2017	2018	2019
평균	1,185	1,196	1,169	1,218	1,228
신장	1,904	1,934	1,955	2,034	2,196
간장	267	176	155	175	160
췌장	852	1,020	1,432	1,230	1,263
심장	203	214	234	228	211
폐	118	116	116	147	234
췌도	1,722	1,205	1,264		562
소장	335			83	

	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
대기자	39	88	123	194	99	120	119	168	245	282
폐이식수술	18	35	37	46	55	64	89	93	92	157
대기 중 사망	17	42	25	52	32	30	46	58	76	82

2 Donor lung procurement

Too many Bad Lungs

- Chest trauma
- Atelectasis
- Pneumonia
- Brain death...Hypotension...Fluid replacement...
  Pulmonary edema

➔ 5~20% 에서만 사용가능

TRANSPLANTATION *:35(7);365-370*

Ideal lung transplant donor criteria

- **Age <55 years**
- ABO compatibility - identical
- Clear chest radiograph
- Pa02 >300 on Fi02 = 1.0, PEEP - 5cm H20
- Tobacco history <20 pack years
- Absence of chest trauma
- No evidence of aspiration/sepsis
- No prior cardiopulmonary surgery
- Sputum gram stain - absence of organisms
- Absence of purulent secretions at bronchoscopy

J Heart Lung Transplant 2000; 19:1199

Extended donor criteria

- **Age <65 years**
- ABO compatibility - compatible
- Clear chest radiograph – unilateral / bronchoscopy / ventilator recruitment maneuver

- Pa02 <300 on Fi02 = 1.0, PEEP - 5cm H20 - try recruitment
- CMV Ab +, DM
- Tobacco history <20 pack years – post transplant lung function / cancer
- Cancer – low grade skin cancer (not melanoma), cervix CIS, CNS tumor (not glioblastoma, not medulloblastoma, no craniotomy, no ventricular shunt, no RT)
- Pulmonary edema, contusion, thromboembolism – contraindication
- Infections

J Heart Lung Transplant 2000; 19:1199

Donor infections limiting transplant

Donors should not be used routinely upon evidence

- Gram-negative bacteremia
- **Mycobacterial infections of the chest**
- Invasive fungal diseases
- Hepatitis C
- Hepatitis B surface antigen-positivity
- HIV/AIDS
- Creutzfeldt-Jakob disease
- West Nile virus
- Severe acute respiratory syndrome (SARS)

J Heart Lung Transplant 2000; 19:1199

2 Donor lung procurement

Allograft size matching

- CXR
- Chest measurement
- **Height**

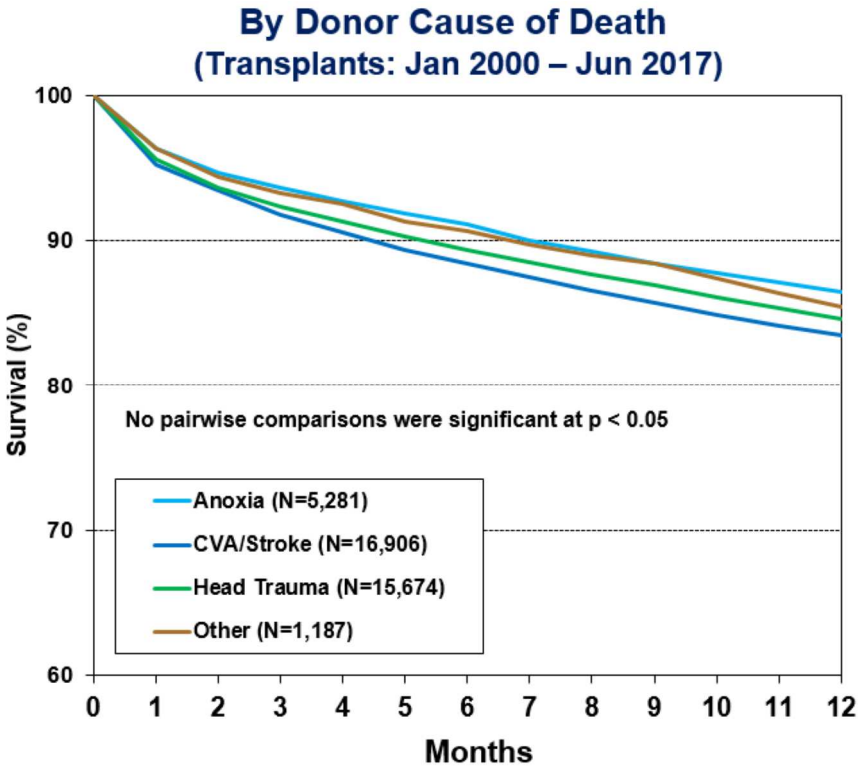
- Predicted TLC for the donor should be within **80% - 120%** of that predicted for the recipient.

- 일반적으로 공급폐의 크기는 수용자의 **폐크기보다 약간 적은 것이 보다 바람직**하다.

2 Donor lung procurement

발생정보

최초내원일시	2022-04-04 21:15
진단명	T-SAH
내원경위	내원 당일 사다리에서 추락하여 머리 부딪혀 119 신고됨. 타 병원 경유하여 본원 응급실 통해 내원함.
뇌사환경	기타사고
뇌사기전	두개내출혈/뇌졸중
뇌사원인	두부외상
사망진단	변사
기타 골절 및 외상	Fx. skull vault, Fx. frontal bone, Fx. zygoma Lt, Fx. mandible Lt, Fx. bof Lt
수술	NONE
심폐소생술	NONE
CRRT	NONE
ECMO	NONE



ISHLT
ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

2 Donor lung procurement

최종 매칭리스트 | 매칭리스트 | 뇌사 기본정보 | **잠재 뇌사정보** | 투약정보 | 검사결과 I | 검사결과 II

과거력

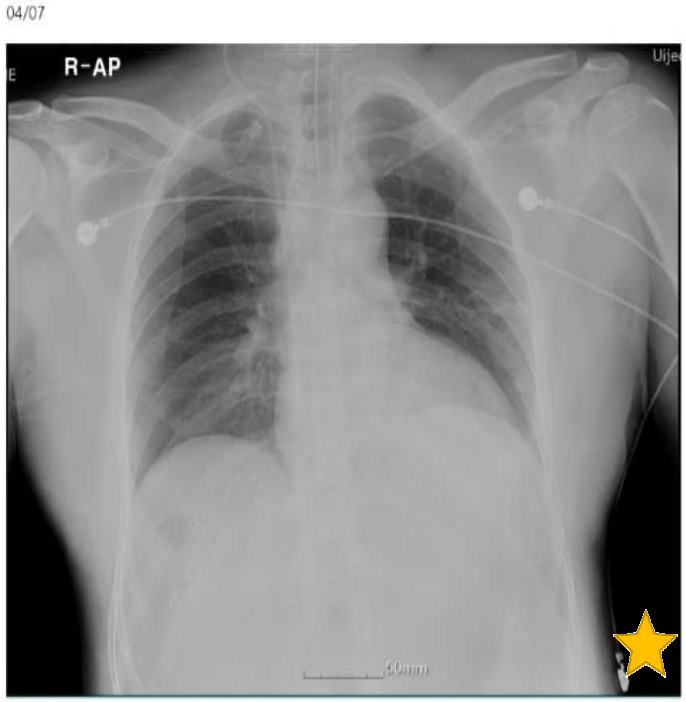
Alcohol	NONE
Tobacco	NONE
고혈압/심혈관계	NONE
당뇨	NONE
AIDS	음성
VDRL	음성
간염	없음
암	none.
결핵/폐질환	none.
기타감염	none.
과거수술	심장 스탠트 삽입술(5-6년전) 2021.01.26 생체간이식 donor
기타	Unstable angina(2VD) -> PCI(2015), old MI(2017)

(U/L / U/L)	39 / 18
Total B (mg/dL)	0.33
CRP (mg/dL)	
CK-MB (μg/L)	
CPK (U/L)	638

동맥가스분석

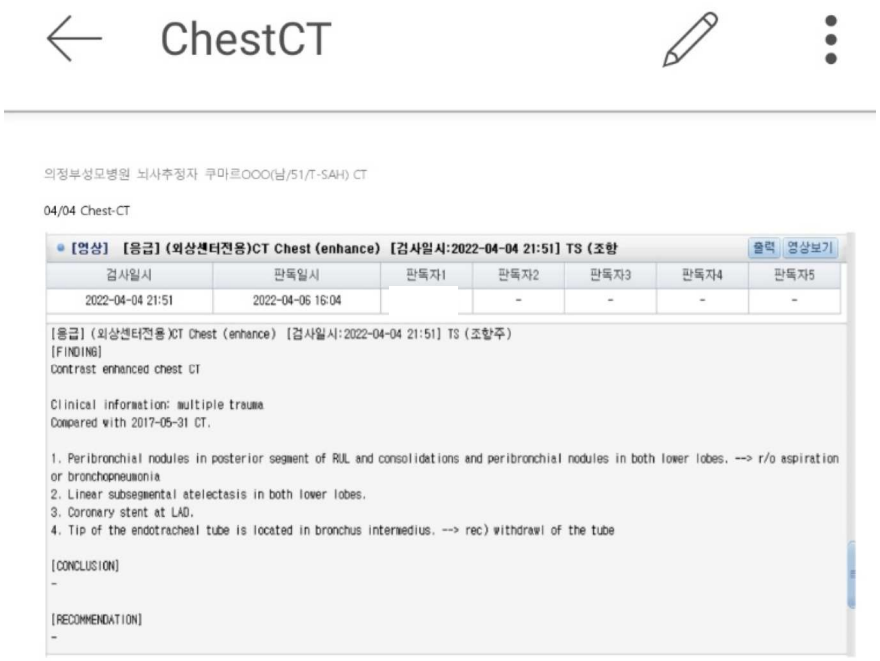
일시	2022-04-07 08:21
PH	7.44
PO2 (mmHg)	550
PCO2 (mmHg)	35.4
O2 Sat. (%)	100
FiO2(%)	100

Chest X-ray



2 Donor lung procurement

Further optional study.....


ChestCT

의정부성모병원 뇌사추정자 쿠마르OOO(남/51/T-SAH) CT

04/04 Chest-CT

[영상] [응급] (외상센터전용)CT Chest (enhance) [검사일시:2022-04-04 21:51] TS (조항

출력 영상보기

검사일시	판독일시	판독자1	판독자2	판독자3	판독자4	판독자5
2022-04-04 21:51	2022-04-05 16:04		-	-	-	-

[응급] (외상센터전용)CT Chest (enhance) [검사일시:2022-04-04 21:51] TS (조항주)
[FINDING]
Contrast enhanced chest CT

Clinical information: multiple trauma
Compared with 2017-05-31 CT.

1. Peribronchial nodules in posterior segment of RUL and consolidations and peribronchial nodules in both lower lobes. --> r/o aspiration or bronchopneumonia
2. Linear subsegmental atelectasis in both lower lobes.
3. Coronary stent at LAD.
4. Tip of the endotracheal tube is located in bronchus intermedius. --> rec) withdrawl of the tube

[CONCLUSION]
-

[RECOMMENDATION]
-

Bronchoscopy

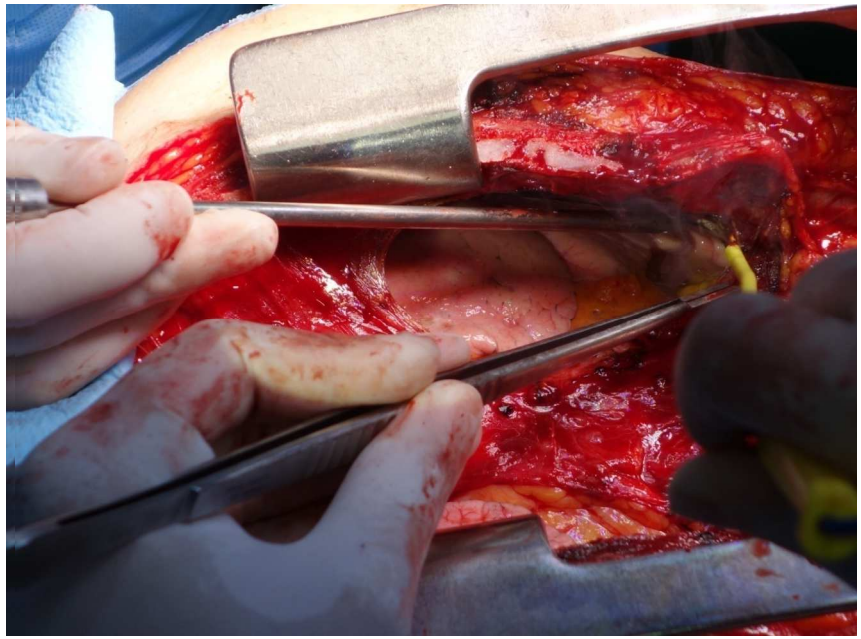
- Screening measure to select potential lung donors
- Only 33% of all brain-dead donors and 62% of ideal donors, based on CXR and arterial blood gas analysis, had normal fiber-optic bronchoscopy.
- 보통, 폐이식 진행 병원에서 시행

Lung procurement technique

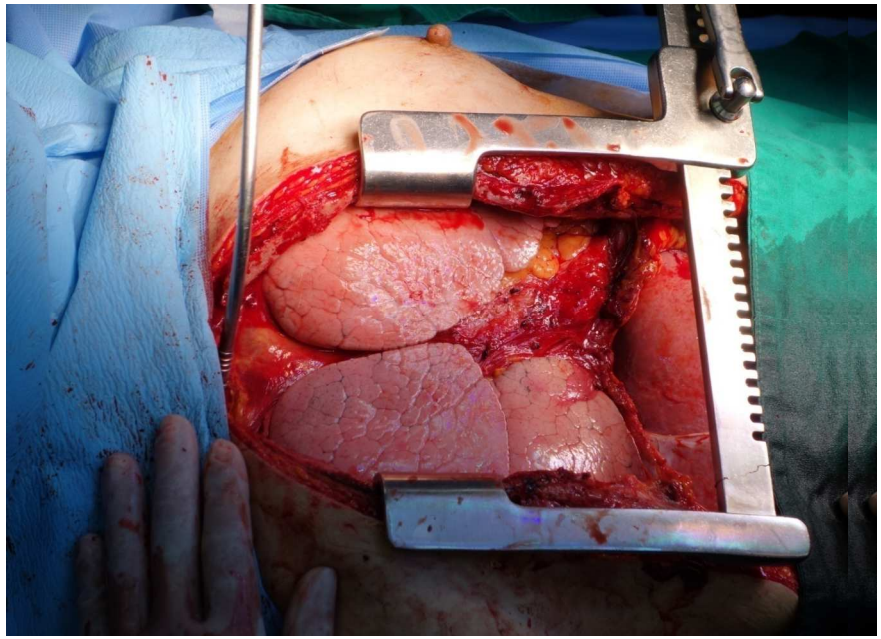
Ventilation	**Tidal volume: 8 to 10 mL per kg, FIO2: 50 percent PEEP: 5 cm H2O**
Anticoagulation (once lungs and heart exposed)	Heparin 250 to 300 units per kg, intravenously
Prostaglandin pretreatment	Prostaglandin E1 (PGE1, Alprostadil) 500 mcg via main pulmonary artery
Flush solution	Low potassium dextran (Perfadex®)
Temperature	4 to 8°C
Antegrade flush	Infuse 50 to 75 mL/kg of flush solution into main pulmonary artery
Cardioplegia solution (only when heart is used for transplantation)	Infuse retrograde from aorta
Topical cooling	Iced saline slush added to pleural and pericardial spaces
Retrograde flush, after removal of heart	Infuse 250 mL of flush solution into each pulmonary vein orifice and vent at pulmonary artery opening

2 Donor lung procurement

DONOR LUNG EXAMINATION

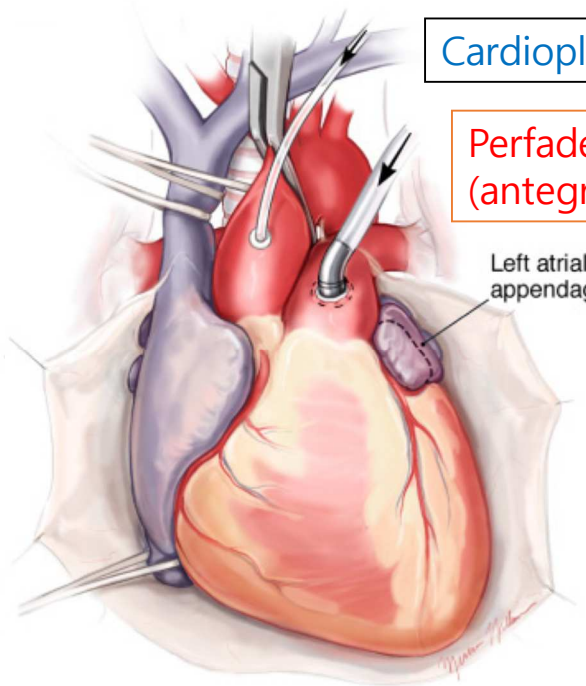


Adhesion? Pulmonary mass?



Compliance test

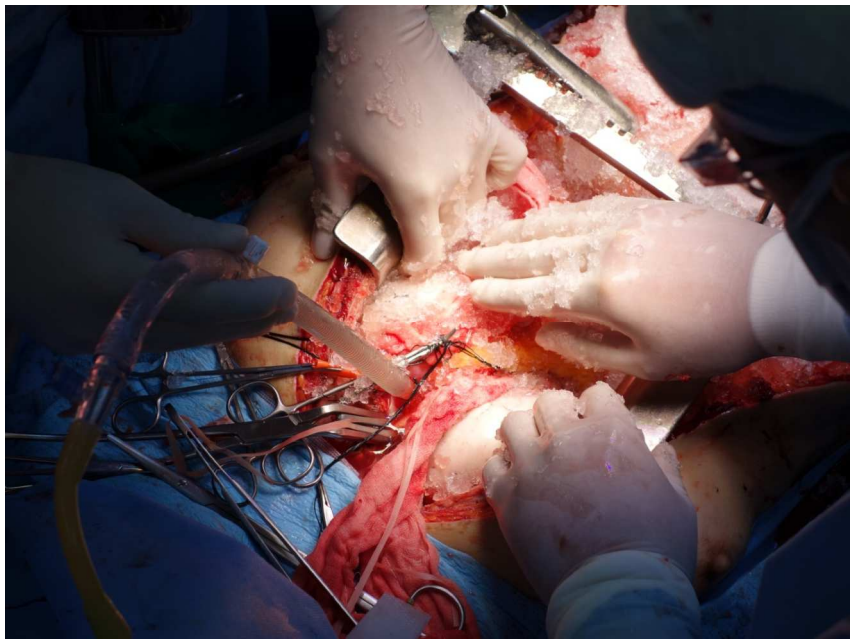
2 Donor lung procurement



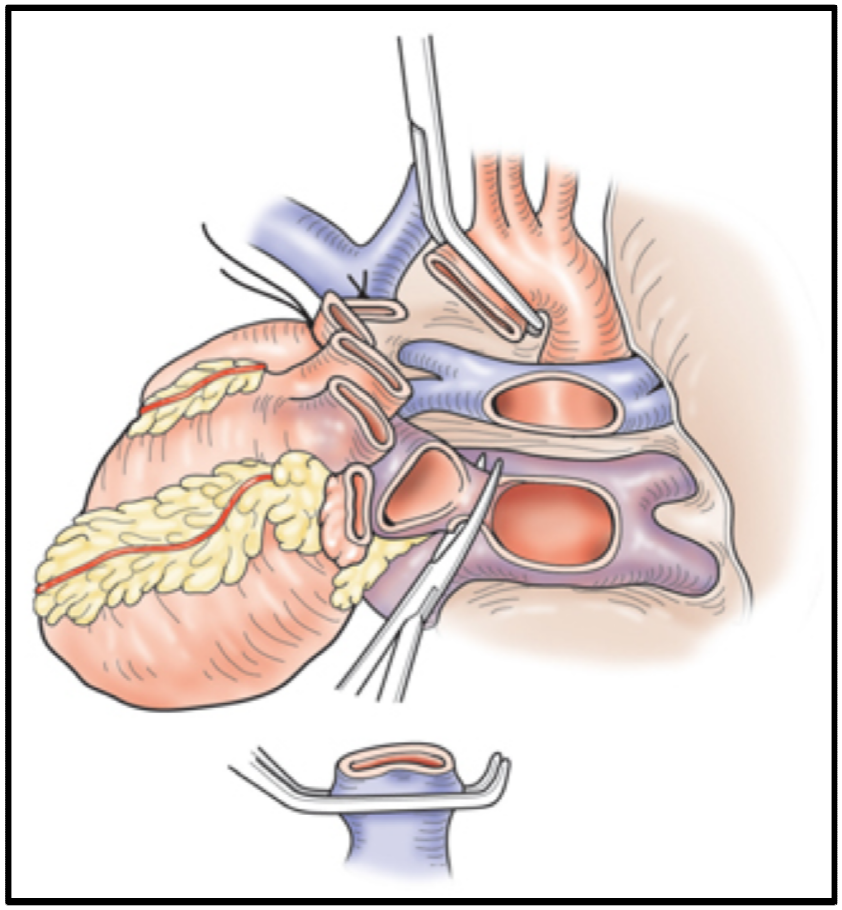
Cardioplegia infusion

Perfadex® solution
(antegrade perfusion)

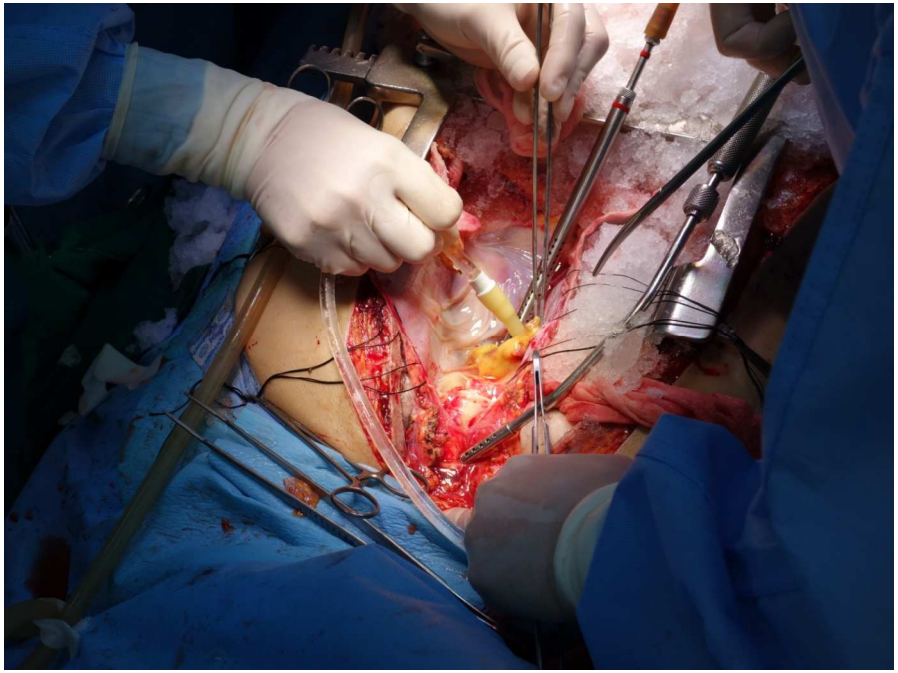
Heparin, PGE1 injection



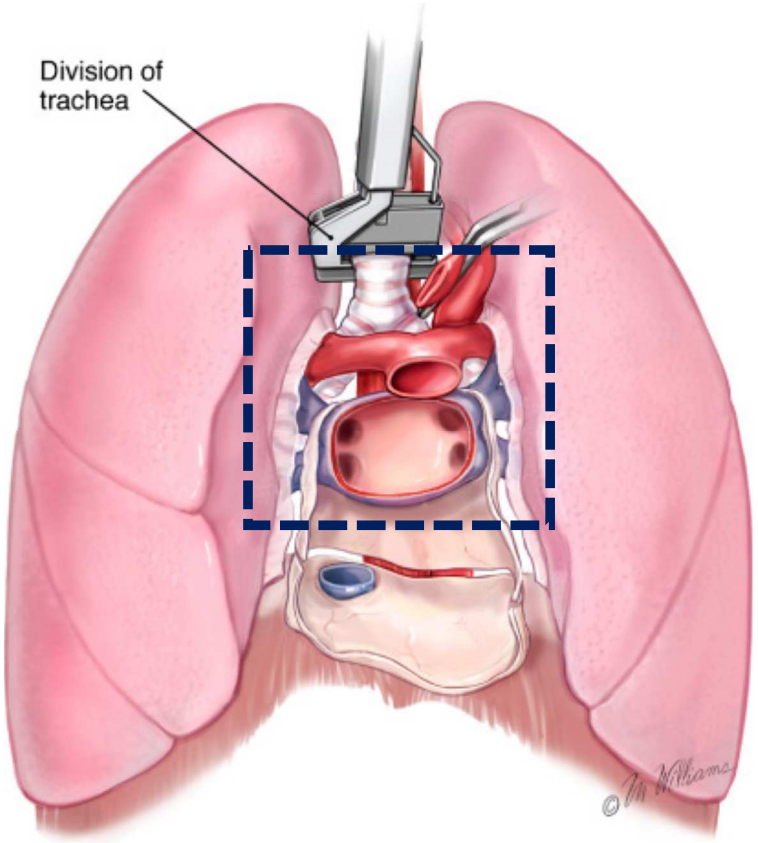
2 Donor lung procurement

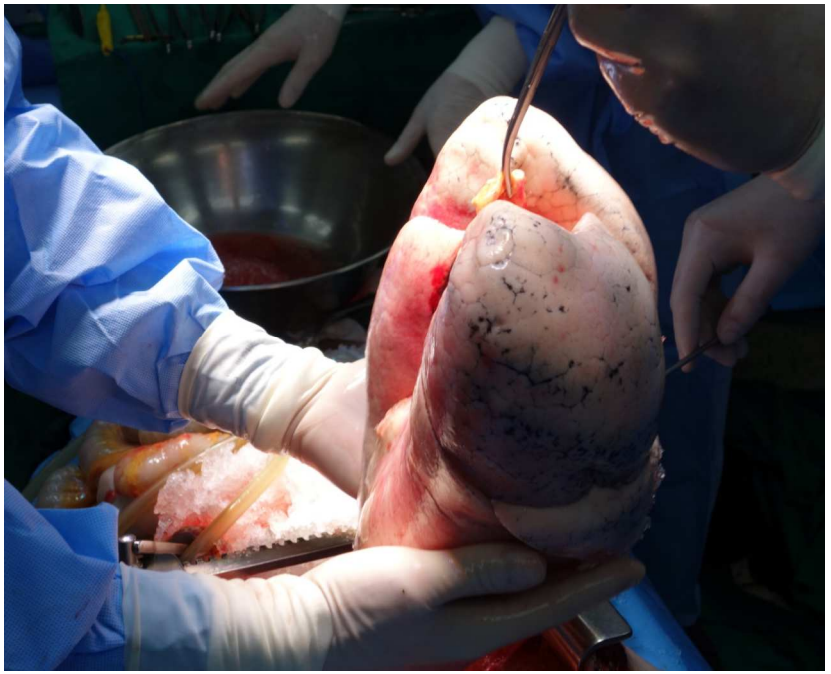


Retrograde perfusion after heart harvesting via pulmonary vein



2 Donor lung procurement





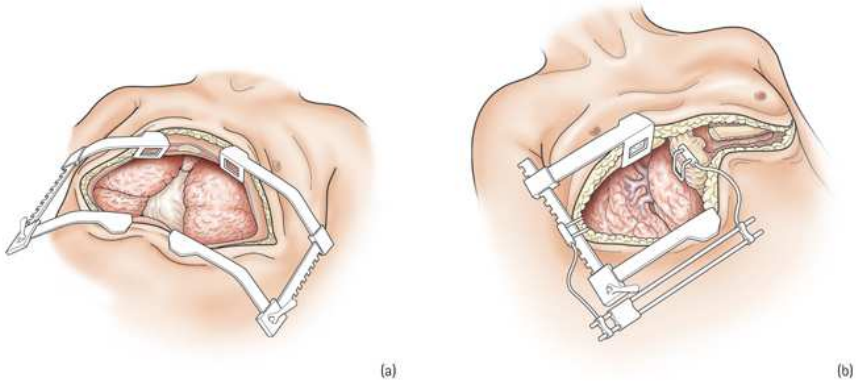
Transportation

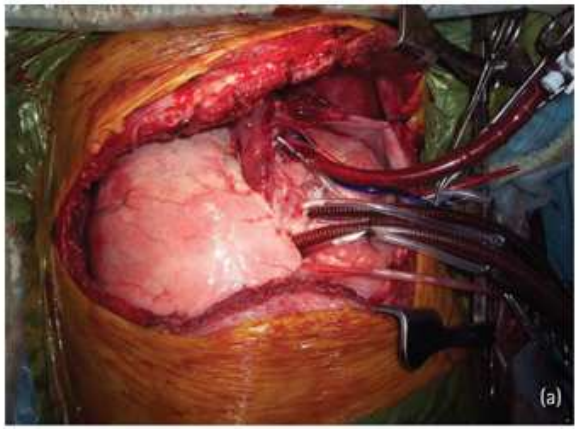
- Lung expansion
  - FiO2 30-50%
  - 50-70% of lung volume
  - Airway pressure 20 cmH2O

- Preservation temperature
  - $4^{o}C$
  - Cold ischemic time less than 8 hours preferred, possibly up to 12

3 Implantation of donor lung

Clamshell incision



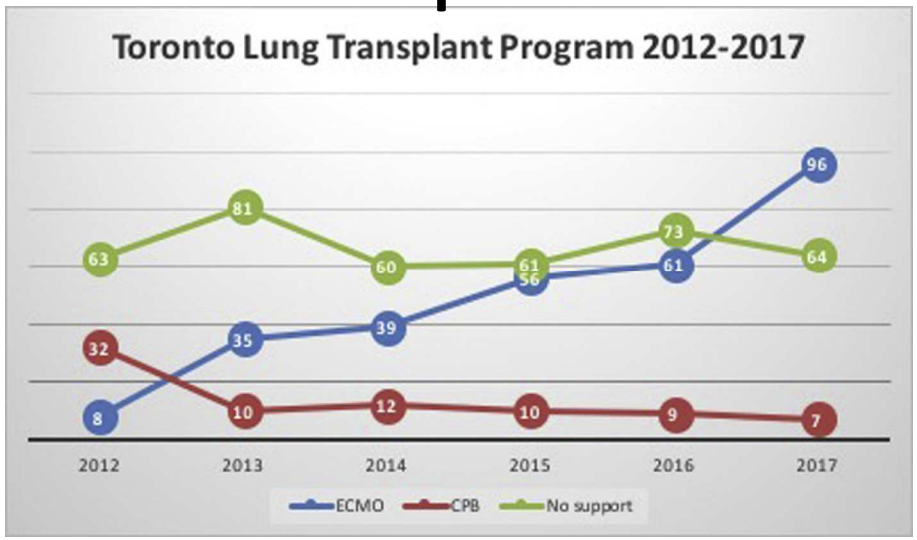


CPB

ECMO

3 Implantation of donor lung

ECMO in Toronto general hospital



- **ECMO**

1) Low dose of heparinization
2) Prolonged use outside the operating room
3) Positive outcomes after lung transplantation
4) Lower the reperfusion injury (both CPB and ECMO)

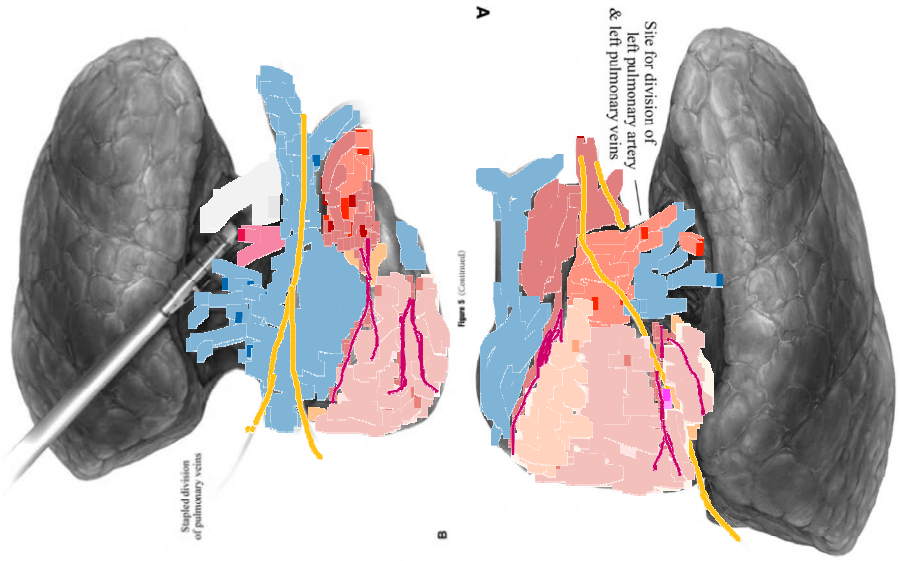
- **CPB**

1) Full-dose heparin

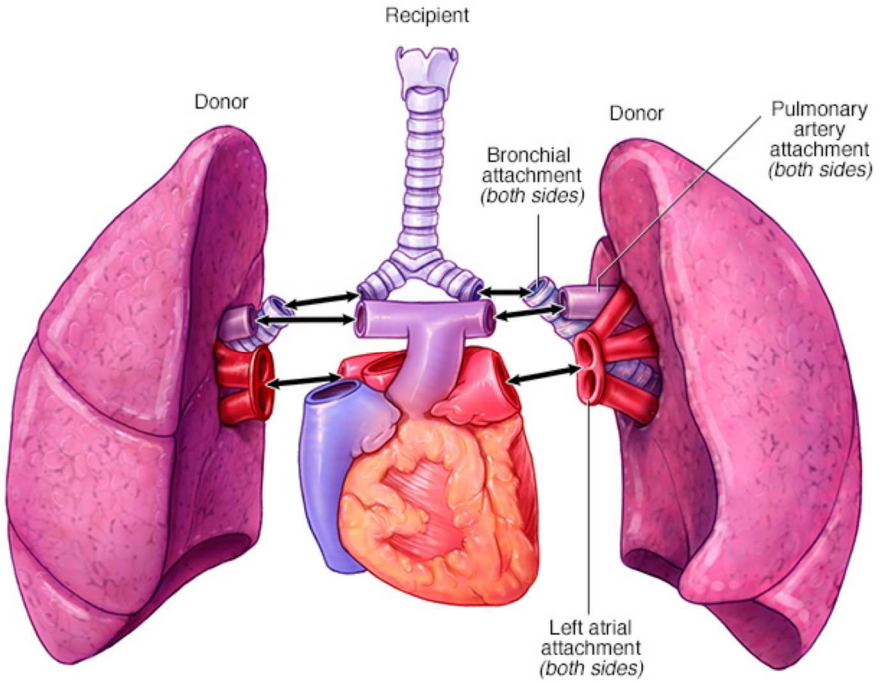
> bleeding and graft dysfunction d/t inflammatory response

3 Implantation of donor lung

Recipient pneumonectomy

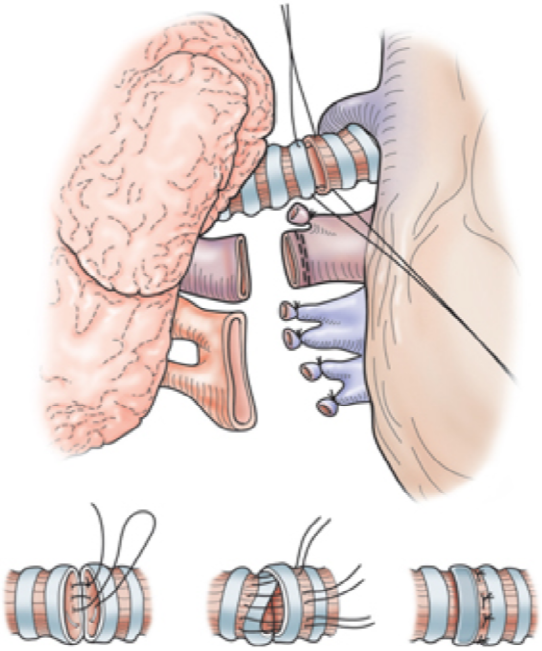


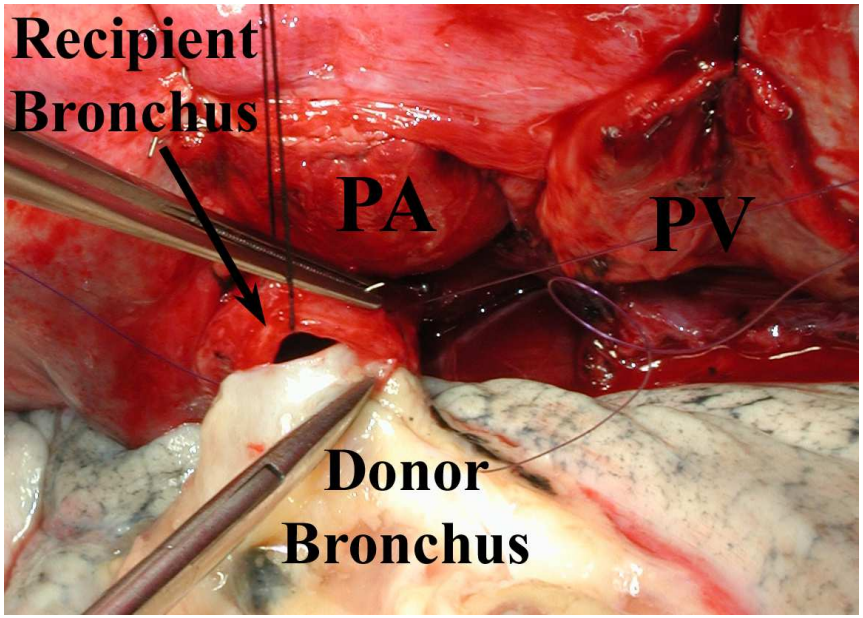
Implantation of the donor lung



3 Implantation of donor lung

Bronchus anastomosis : continuous or interrupted, PDS 4/0

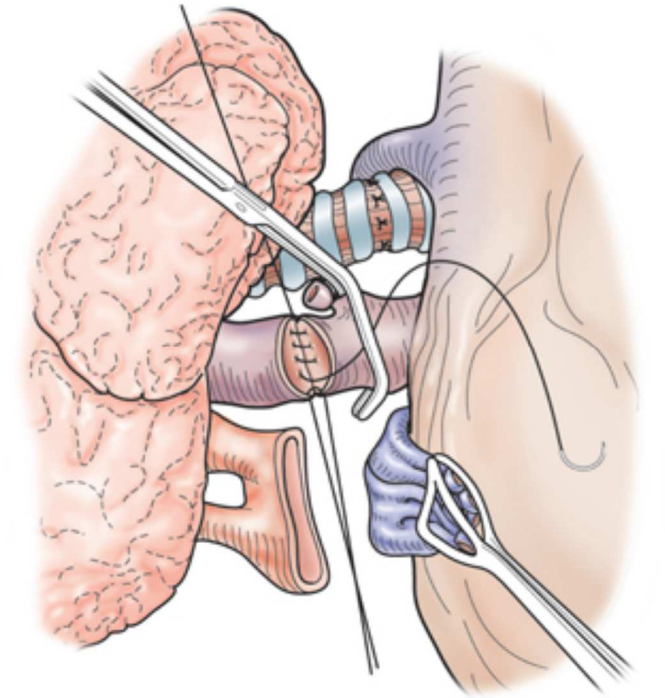


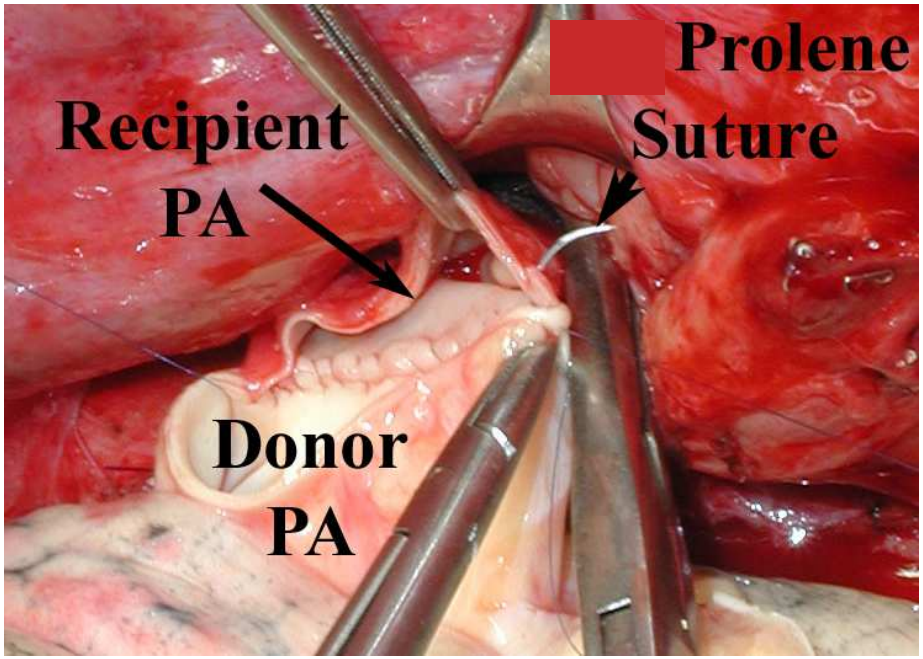


air leakage test and bronchoscopy

3 Implantation of donor lung

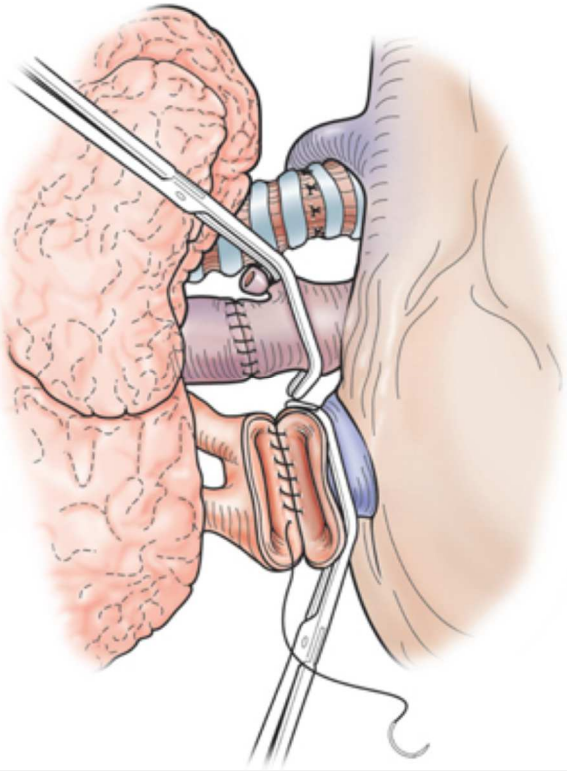
PA anastomosis : continuous running suture, prolene 5/0

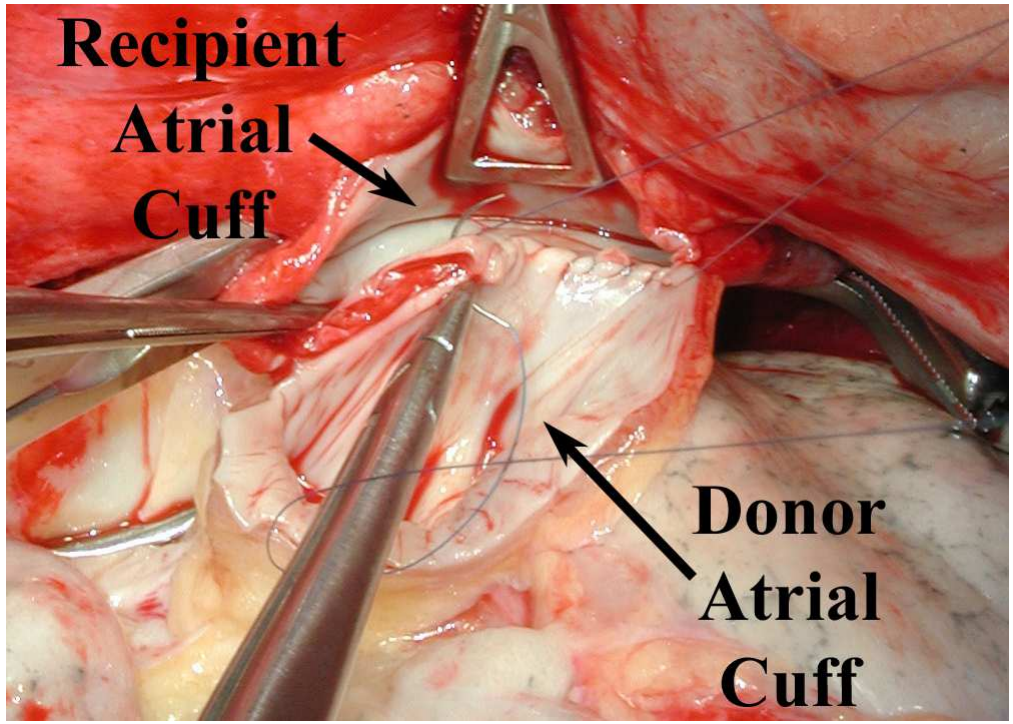




3 Implantation of donor lung

PV anastomosis : continuous running suture, prolene 4/0

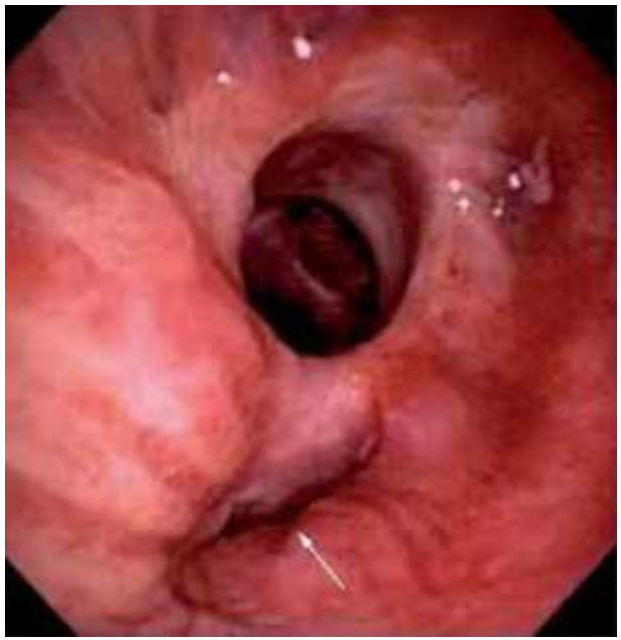




3 Implantation of donor lung

Airway complication

- Possible causes of failure included medication, infection, rejection, and ischemia resulting from loss of the bronchial arterial supply.
- Mostly because of donor bronchial ischemia
- Revascularization of the donor airway occurs over 2 to 4 weeks.



3 Lung transplantation – AIRWAY COMPLICATION

- Donor and recipient characteristics : Height mismatch
- Hypoperfusion due to hypotension
- Right-sided anastomoses : only 1 bronchial artery
- Mechanical ventilation : high PEEP
- Immunosuppression : mTOR inhibitors
- Operation
  - Avoid tracheal anastomosis
  - Minimizing the length of donor bronchus, avoid skeletonization of donor bronchus
  - Avoid single continuous running suture
    - Creating the anastomosis at the secondary carina.
    - A running suture is placed along the membranous portion of the bronchi, followed by figure-of-eight stitches into the cartilaginous membrane.

3 Lung transplantation : Immunosuppressant

- **Induction :** To reduce the risk of acute rejection
  - Interleukin 2 receptor antagonists
    [Daclizumab and basilixmab (in SNUBH, Simulect)]
  - Anti-thymocyte globulin (ATG)
- **Maintenance**

: Life long immunosuppressive therapy that is given to prevent both acute and chronic rejection

1) Calcineurin inhibitor (Cyclosporine, in SNUBH, tacrolimus),

2) Antiproliferative agent
[MMF, Azathioprine, in SNUBH, mycophenolate sodium (myrept)]

3) Corticosteroids (in SNUBH, methyPd 0.5mg/kg).

3 Lung transplantation : Antimicrobial therapy

- Bacterial prophylaxis

- HSV prophylaxis > acyclovir
- PCP > Cotrimoxazole
- Candida > nystatin
- CMV > Gancyclovir

SUMMARY

1. *Although survival following lung transplantation continues to improves, it remains the worst outcome of all solid organ transplantation.*

1. *Both chronic resection (m/c BOS)and infection occur more commonly and earlier in lung allografts compared with other solid organ transplants.*

1. *Current standard approach to implantation is for single or sequential bilateral implantation by a ′clamshell incision′under ECMO. The anastomosis is conducted from posterior to anterior in the following order: bronchus, pulmonary artery, atrium (pulmonary vein).*

Thank you for your attention

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