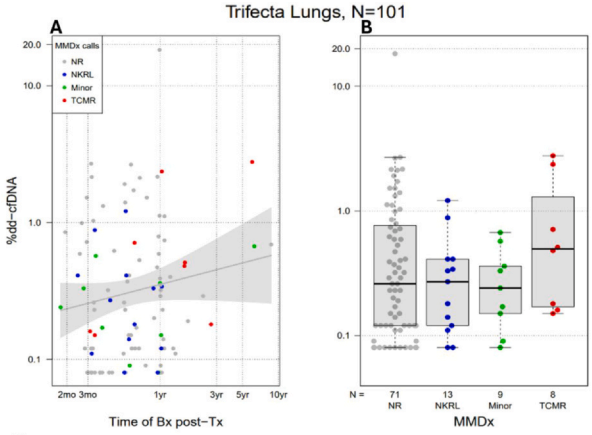
Conclusion: In these first 101 TBBs available for analysis, dd-cfDNA strongly correlated with injury genes and extracellular matrix remodeling. Whether these genes anticipate future CLAD will be of interest in long term follow-up. More TCMR cases are needed to define its relationship with dd-cfDNA.



C

Gene Ontology enrichment analysis using top 200 genes positively correlated with %dd-cfDNA in 101 TBBs			
Description	p-value	q-value	Gene IDs for top 6 genes ranked by correlation with dd-cfDNA
collagen-containing extracellular matrix	7E-37	2E-34	MFAP2/IGFBP7/EGFLAM/ASPN/COL14A1/COL4A1/SPARC
extracellular matrix structural constituent	8E-34	3E-31	MFAP2/IGFBP7/ASPN/COL14A1/COL4A1/SPARC
basement membrane	1E-17	1E-15	EGFLAM/COL4A1/SPARC/EGFL6/NID1/THBS4
extracellular matrix organization	1E-17	1E-14	EGFLAM/COL14A1/COL4A1/MMP7/EGFL6/NID1
extracellular structure organization	1E-17	1E-14	EGFLAM/COL14A1/COL4A1/MMP7/EGFL6/NID1
external encapsulating structure organization	2E-17	1E-14	EGFLAM/COL14A1/COL4A1/MMP7/EGFL6/NID1
extracellular matrix structural constituent conferring tensile strength	1E-14	2E-12	COL14A1/COL4A1/COL6A3/COL1A2/COL3A1/COL5A2
collagen fibril organization	1E-12	7E-10	COL14A1/COL1A2/COL3A1/COL5A2/SFRP2/LOX
collagen trimer	1E-12	1E-10	COL14A1/COL4A1/COL6A3/COL1A2/COL3A1/COL5A2
endoplasmic reticulum lumen	2E-12	1E-10	IGFBP7/COL14A1/COL4A1/VCAN/COL6A3/COL1A2
complex of collagen trimers	9E-12	4E-10	COL4A1/COL1A2/COL3A1/COL5A2/COL1A1/COL5A1
fibrillar collagen trimer	5E-10	2E-08	COL1A2/COL3A1/COL5A2/COL1A1/COL5A1/COL11A1
banded collagen fibril	5E-10	2E-08	COL1A2/COL3A1/COL5A2/COL1A1/COL5A1/COL11A1
extracellular matrix binding	7E-10	8E-08	SPARC/NID1/BGN/OLFML2B/COL11A1/SMOC2
glycosaminoglycan binding	2E-08	1E-06	EGFLAM/STAB2/CEMIP/VCAN/THBS4/BGN
collagen binding	2E-08	2E-06	COL14A1/SPARC/NID1/PODN/LOX/PCOLCE
platelet-derived growth factor binding	4E-08	2E-06	COL4A1/COL1A2/COL3A1/COL1A1/COL5A1
response to transforming growth factor beta	5E-08	2E-05	NREP/ASPN/COL1A2/TGFB3/SPRY1/COL3A1
extracellular matrix structural constituent conferring compression resistance	5E-08	3E-06	ASPN/VCAN/BGN/OGN/PODN/FMOD
growth factor binding	1E-07	4E-06	IGFBP7/COL4A1/COL1A2/TGFB3/COL3A1

D

Significant correlations of gene sets with %dd-cfDNA in TBBs (N=101) (of 34 gene sets)				
	Gene sets	Correlation	p-value	FDR
Top POSITIVELY correlated gene sets	Fibrillar collagens (COLA1356)	0.33	9.1E-4	0.03
	Injury-induced (IRITD5)	0.31	1.5E-3	0.03
	Injury-induced (IRRAT30)	0.31	1.5E-3	0.03
	Fibrillar collagens (FICOL)	0.30	2.4E-3	0.04
	Mast cell transcripts (MCAT)	0.24	0.02	0.21
	Genes increased in CLAD time corrected (CLADup)	0.23	0.02	0.21
	Injury-induced (IRITD3)	0.21	0.04	0.27
Top NEGATIVELY correlated gene sets	Normal lung genes (SLC) LT2	-0.14	0.16	0.61
	Normal lung genes LT3	-0.14	0.18	0.61
	Normal lung genes LT1	-0.13	0.19	0.61
	Normal lung genes (SLC) LT4	-0.12	0.22	0.61

Figure 1. Dd-cfDNA levels and the relationship to time of biopsy post-transplant (**A**) and with no rejection (NR), minor abnormalities (Minor), NK cell enriched rejection-like (NKRL) and T cell mediated (TCMR) rejection MMDx calls (**B**). Gene ontology (GO) enrichment analysis for the top 200 genes positively correlated with %dd-cfDNA **(C)**. Spearman coefficient correlations between %dd-cfDNA and gene sets in 101 TBBs (**D**).

(194)

Changes in Hyperpolarized Xenon-129 MRI-Based Pulmonary Function Metrics Following Lung Transplantation

K. Ruppert,[1] H. Hamedani,[1] C. Bermudez,[2] M. Crespo,[3] A. Courtwright,[3] J. Diamond,[3] P. Peitl Gregorio,[2] E. Cantu,[2] L. Loza,[1] J. Chen,[1] M. Ismail,[1] and R.R. Rizi.[1] [1]Department of Radiology, University of Pennsylvania, Philadelphia, PA; [2]Division of Cardiac Surgery, University of Pennsylvania, Philadelphia, PA; [3]Division of Pulmonary Medicine and Critical Care, University of Pennsylvania, Philadelphia, PA

Purpose: Lung allografts are subject to multifactorial subclinical injuries driven by both immune and non-immune processes. This study investigates differences in lung function and structure among apparently healthy subjects 3-24 months post-bilateral lung transplantation (LTx), late-stage chronic obstructive pulmonary disease (COPD) patients, and healthy control subjects (HCS).

Methods: This study included 27 healthy LTx subjects [15 (56%) male, 12 (44%) female, age 56 ± 12.6 yrs], 8 COPD patients [6 (75%) male, 2 (25%) female, age 68 ± 6.6 yrs], and 17 HCS [13 (76%) male, 4 (24%) female, age 42 ± 14.5 yrs]. We measured apparent diffusion coefficient (ADC)—reflecting alveolar dimensions—red blood cell (RBC)-to-membrane (Mem) signal ratio, and alveolar septal wall thickness (aSWT) using MRI during a 6-second breath hold following inhalation of 0.5 L of hyperpolarized xenon-129.

Results: Figure 1A shows that alveolar gas ADC in the LTx subjects (0.046 ± 0.0063 cm^2/s) was similar to that of HCS (0.046 ± 0.0053 cm^2/s). The emphysematous COPD cohort, potentially representing a large subgroup of LTx subjects prior to transplantation, exhibited a much higher ADC (0.085 ± 0.0038 cm^2/s). However, the RBC:Mem ratio (Figs. 1A and 1B), reflecting the amount of xenon bound to hemoglobin relative to the volume dissolved in lung tissue, was significantly lower in LTx subjects (20.1 ± 5.0%) compared to HCS (39.1 ± 8.3%, $p < 0.001$) and even below the reduced values seen in COPD patients (27.1 ± 4.2%, $p = 0.0016$). As shown in Fig. 1B, LTx subjects also exhibited increased aSWT (11.5 ± 1.38 μm) compared to HCS (10.0 ± 0.83 μm, $p < 0.001$), potentially indicating inflammatory processes, though at a lower level than the COPD cohort (13.8 ± 1.57 μm, $p < 0.001$).

Conclusion: This MRI-based study reveals previously undetected pulmonary abnormalities in LTx subjects, even when they appear healthy. These findings suggest that LTx recipients may exhibit underlying structural and functional changes in the absence of overt clinical symptoms.

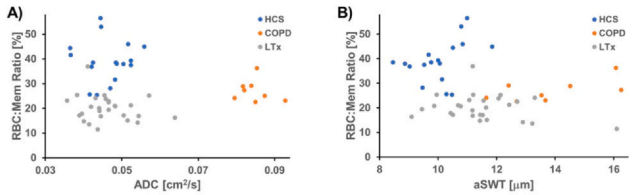


Figure 1. A) Red blood cell to membrane (RBC:Mem) ratio over the apparent diffusion coefficient (ADC) for healthy control subjects (HCS), COPD patients, and lung transplant recipients (LTx). B) RBC:Mem ratio over the alveolar septal wall thickness (aSWT) in the same cohorts as in (A).

(195)

The Impact of Functional Warm Ischemia Time on Procurement and Preservation Technique in DCD Heart Transplantation

B.E. Ferrell,[1] R. Zhu,[2] A. Dweck,[3] K. Hershenhouse,[1] S.M. Spindel,[1] S. Madan,[4] S. Patel,[4] U. Jorde,[4] S. Forest,[1] and D. Goldstein.[1] [1]Department of Cardiothoracic and Vascular Surgery, Montefiore Medical Center, Bronx, NY; [2]Department of Cardiovascular and Thoracic Surgery, Staten Island University Hospital, Staten Island, NY; [3]Albert Einstein College of Medicine, Bronx, NY; [4]Department of Cardiology, Montefiore Medical Center, Bronx, NY

Purpose: Heart transplantation following donation after circulatory death (DCD HT) has led to a significant increase in transplantation volume. Procurement and preservation techniques including direct procurement and perfusion (DPP) and normothermic regional perfusion (NRP) are utilized in DCD donation. Functional warm ischemia (fWIT) precedes organ procurement and subjects the donor heart to ischemic injury. We aimed to evaluate the impact of fWIT on outcomes after DPP and NRP procurement in DCD HT.

Methods: The United Network for Organ Sharing registry was queried for adults (≥ 18 years) undergoing isolated, primary HT with a DCD donor from 2019 - 2023. fWIT was defined as start of the agonal phase to donor cross clamp in DPP retrievals, and from start of the agonal phase to donor brain death plus 10 minutes in NRP cases. Transplants were stratified by fWIT ≤ 30 minutes (T1) and > 30 minutes (T2).

Results: A total of 992 transplants were stratified into T1 (738, 74%) and T2 (254, 26%). The T1 group had a shorter fWIT (22 vs 43 minutes, $p < 0.0001$) and longer total preservation time (5.3 vs 4.5 hours, p=0.01). DPP was more commonly utilized in the T1 cohort (528 (72%) vs 143 (63%) $p < 0.0001$). There was no difference in distance traveled between groups (T1: 324 vs T2: 313 miles, p=0.74). Unadjusted Kaplan-Meier survival and cox regression analysis demonstrated no difference in 1 year survival in the T1 cohort between NRP and DPP procurement techniques (log rank p = 0.07, HR: 1.59 [0.96-2.65]). In the T2 cohort, there was a significant decrease in survival when DPP was utilized (log rank p = 0.002, HR: 3.23 [1.54-6.75]). There was no difference in post-operative dialysis (135 (18%) vs 40 (16%), p=0.16), stroke (28 (4%) vs 14 (6%), p=0.24), or pacemaker (6 (1%) vs 6 (2%), p=0.05) between the T1 and T2 cohorts.

Conclusion: In prolonged fWIT (> 30 minutes) in DCD HT, utilization of NRP appears superior to DPP and is associated with improved one-year survival.

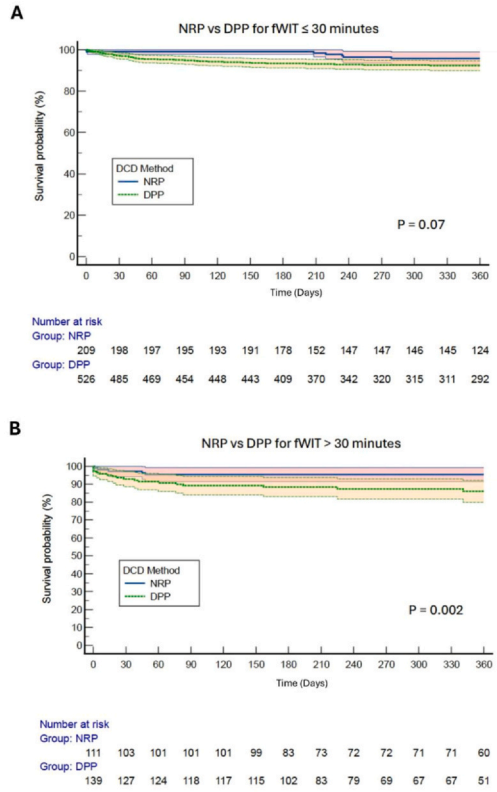


Figure 1: Kaplan Meier survival curves with fWIT **(A)** ≤ 30 minutes and **(B)** > 30 minutes stratified by procurement technique (NRP vs DPP) in DCD heart transplantation

(196)

Global Outcomes with Extended Criteria Donors When Preserved at 4-8°C: An Updated Analysis of the International GUARDIAN Heart Registry

R. Moayedifar,[1] A. Eixeres Esteve,[2] Y. Shudo,[3] M. Kawabori,[4] R. Venkateswaran,[5] S. Silvestry,[6] J. Schroder,[7] H. Mächler,[8] D. Meyer,[9] J. Bustamante-Munguira,[10] D. D'Alessandro,[11] and A. Zuckermann.[12]
[1]Medical University Vienna, Vienna, Austria; [2]12 de Octubre, Madrid, Spain; [3]Stanford University, Stanford, CA; [4]University of Kentucky, Lexington, KY; [5]Wythenshawe Hospital, Manchester, United Kingdom; [6]Banner Health, University of Arizona, Tucson, AZ; [7]Duke University Medical Center, Durham, NC; [8]Medical University of Graz, Graz, Austria; [9]Baylor Scott and White Health, Baylor University Medical Center, Dallas, TX; [10]University Hospital of Valladolid, Valladolid, Spain; [11]MGH, Boston, MA; [12]Medical University of Vienna, Vienna, Austria

Purpose: The rising demand for heart transplants amid a limited donor supply highlights the need to expand the donor pool. Use of a static controlled hypothermic transport system (SCTS) has previously shown significant clinical benefits, as demonstrated in the GUARDIAN-Heart Registry. Following the EXPAND OCS trial, we aim to assess the impact of SCTS on recipient outcomes using extended criteria donors, particularly in the EU, where these donors are more commonly utilized.
Methods: A total adults 568 adults from 25 centers in the US and Europe SCTS (N=357) or historic ice storage (ICE, N=211) enrolled in the GUARDIAN-heart registry were found to meet the modified EXPAND OCS Trial criteria as extended criteria donors (see Table).
Results: There were a few baseline differences among recipients in the 2 cohorts, most notably both distance traveled and total ischemic time was significantly greater in SCTS, and significantly more donor hearts in the SCTS cohort were bridged with ECMO, although durable VADs were more frequent in the ICE cohort (see Table). Post-transplant MCS utilization, PGD, severe PGD and severe RVD were all significantly reduced in hearts preserved using SCTS. Propensity matching using the extended donor criteria resulted in similar baseline characteristics, including durable VADs and ECMO, yet the post-transplant significant benefits remained.
Conclusion: This global subgroup analysis of the GUARDIAN registry demonstrates that SCTS at 4-8°C can be used to optimize post-transplant outcomes when using extended criteria donors, with low post-transplant adverse events despite significantly longer ischemic times.

Table:

	Overall			Propensity Matched#		
	ICE	SCTS		ICE	SCTS	
	n = 211	n = 357	*p-value*	n = 185	n = 185	*p-value*
Donor Inclusion Criteria						
>4h Total Ischemic Time	**106 / 211 (50.2%)**	**253 / 357 (70.9%)**	**<0.001**	106 / 185 (57.3%)	107 / 185 (57.8%)	>0.99
>2h Total Ischemic Time AND						
Age > 55 years	18 / 211 (8.5%)	26 / 357 (7.3%)	0.63	14 / 185 (7.6%)	14 / 185 (7.6%)	>0.99
Downtime > 20 mins	37 / 211 (17.5%)	56 / 357 (15.7%)	0.56	29 / 185 (15.7%)	29 / 185 (15.7%)	>0.99
LVEF 40-50%	44 / 211 (20.9%)	61 / 357 (17.1%)	0.27	38 / 185 (20.5%)	37 / 185 (20.0%)	>0.90
LVPW 12-16 mm	**30 / 211 (14.2%)**	**31 / 357 (8.7%)**	**0.049**	21 / 185 (11.4%)	21 / 185 (11.4%)	>0.99
Luminal Irregularities	5 / 211 (2.4%)	13 / 357 (3.6%)	0.47	3 / 185 (1.6%)	3 / 185 (1.6%)	>0.99
Donor Characteristics						
Donor Age (years)	35.4 ± 12.2	35.2 ± 11.1	0.83	34.8 ± 12.2	35.0 ± 11.5	0.90
Donor BMI (kg/m²)	28.4 ± 6.7	28.2 ± 6.9	0.71	27.8 ± 6.3	28.4 ± 7.4	0.39
Recipient Characteristics						
Recipient Age (years)	53.7 ± 11.7	55.6 ± 12.6	0.069	53.5 ± 11.9	55.6 ± 12.6	0.096
Recipient BMI (kg/m²)	27.7 ± 4.6	27.7 ± 4.8	0.93	27.5 ± 4.6	27.9 ± 4.8	0.44
Implantable VAD	**87 / 211 (41.2%)**	**97 / 357 (27.2%)**	**<0.001**	65 / 185 (35.1%)	66 / 185 (35.7%)	>0.99
Temporary IABP	36 / 211 (17.1%)	75 / 357 (21.0%)	0.27	34 / 185 (18.4%)	36 / 185 (19.5%)	0.89
Temporary ECMO/VAD	**15 / 211 (7.1%)**	**59 / 357 (16.5%)**	**0.001**	15 / 185 (8.1%)	18 / 185 (9.7%)	0.72
Waitlist Days	**178.0 ± 302.5**	**122.1 ± 324.5**	**0.039**	163.6 ± 298.7	136.8 ± 323.3	0.41
Match Characteristics						
F/M Mismatch	29 / 211 (13.7%)	45 / 357 (12.6%)	0.70	23 / 185 (12.4%)	28 / 185 (15.1%)	0.55
Distance to Organ (miles*)	**355 ± 301**	**561 ± 395**	**<0.001**	**385 ± 306**	**534 ± 375**	**<0.001**
Total Ischemic Time (hours)	**3.7 ± 0.9**	**4.3 ± 0.9**	**<0.001**	3.9 ± 0.9	4.0 ± 0.9	0.070
Average Temperature	**NA (<0°C)**	**5.5 ± 2.4°C**	**--**	NA (<0°C)	5.6 ± 2.9	--
Post-transplant Outcomes						
All Post Tx MCS	**61 / 211 (28.9%)**	**68 / 357 (19.0%)**	**0.009**	**56 / 185 (30.3%)**	**38 / 185 (20.5%)**	**0.042**
Cardioversion	36 / 211 (17.1%)	46 / 357 (12.9%)	0.18	34 / 185 (18.4%)	20 / 185 (10.8%)	0.055
PGD	**57 / 211 (27.0%)**	**60 / 357 (16.8%)**	**0.005**	**49 / 185 (26.5%)**	**29 / 185 (15.7%)**	**0.015**
PGD Severe	**29 / 211 (13.7%)**	**26 / 357 (7.3%)**	**0.018**	**26 / 185 (14.1%)**	**12 / 185 (6.5%)**	**0.025**
RV-PGD	9 / 211 (4.3%)	7 / 354 (2.0%)	0.12	8 / 185 (4.3%)	2 / 185 (1.1%)	0.10
RV Normal at 24 hours	**77 / 191 (40.3%)**	**168 / 306 (54.9%)**	**0.002**	**65 / 168 (38.7%)**	**94 / 165 (57.0%)**	**<0.001**
RV Severely diminished	**27 / 191 (14.1%)**	**16 / 306 (5.2%)**	**<0.001**	**26 / 168 (15.5%)**	**7 / 165 (4.2%)**	**<0.001**
ICU LOS	12.7 ± 18.5	11.2 ± 16.0	0.31	12.1 ± 16.4	11.7 ± 15.2	0.84
Median (min, max)	6.0 (1.0, 128.0)	6.0 (0.0, 137.0)	0.19	6.0 (1.0, 110.0)	6.0 (1.0, 92.0)	0.73
Total Hospital LOS	29.4 ± 30.9	26.8 ± 28.1	0.31	27.9 ± 28.0	28.3 ± 30.1	0.88
Median (min, max)	20.0 (7.0, 268.0)	18.0 (6.0, 294.0)	0.061	19.0 (7.0, 268.0)	19.0 (7.0, 294.0)	0.72
In-hospital Survival	201 / 211 (95.3%)	350 / 357 (98.0%)	0.075	176 / 185 (95.1%)	180 / 185 (97.3%)	0.41
1-year Survival	194 / 211 (91.9%)	309 / 334 (92.5%)	0.87	171 / 185 (92.4%)	173 / 184 (94.0%)	0.68
2-year Survival	181 / 208 (87.0%)	261 / 294 (88.8%)	0.58	160 / 182 (87.9%)	161 / 180 (89.4%)	0.74

Abbreviations: BMI = body mass index; SCTS = (Paragonix) SherpaPak cardiac transport system; ECMO = extracorporeal membrane oxygenation; F/M mismatch = female to male mismatch; IABP = intra-aortic balloon pump; LVEF = left ventricular ejection fraction; LVPW = left ventricular posterior wall; LOS = length of stay; MCS = mechanical circulatory support; PGD = primary graft dysfunction; PHM = predicted heart mass; Tx = transplant; VAD = ventricular assist device.
Continuous data presented as average ± standard deviation.
Cohorts were propensity matched using the extended criteria variables.
* miles are in nautical miles.

(197)

A Decade of Donation After Circulatory Death Heart Transplantation: Long Term Outcomes from the Australian Experience

Y. Joshi,[1] C. MacLean,[2] K. Wang,[2] J. Villanueva,[3] L. Gao,[3] S. Scheuer,[1] C. Soto,[4] M. Connellan,[1] A. Watson,[1] A. Iyer,[1] E. Granger,[1] K. Muthiah,[5] P. Jansz,[1] and P. MacDonald.[5] [1]Cardiothoracic Surgery, St Vincent's Hospital, Sydney, Darlinghurst, Australia; [2]University of New South Wales, Sydney, Australia; [3]Victor Chang Cardiac Research Institute, Darlinghurst, Australia; [4]Department of Perfusion, St Vincent's Hospital, Sydney, Darlinghurst, Australia; [5]Cardiology, St Vincent's Hospital, Sydney, Darlinghurst, Australia

Purpose: Heart transplantation (HT) from donation after circulatory death (DCD) donors successfully expands the donor pool with excellent short term survival outcomes globally. Our institution performed the world's first DCD heart transplant 10yrs ago using normothermic machine perfusion (NMP). We evaluate the long term survival outcomes of DCD heart transplantation (DCD-HT), as well as the incidence of cardiac allograft vasculopathy (CAV), which has yet to be explored.
Methods: All heart transplants in our institution over a 10year period from January 2014-July 2024 were included. Results from DCD-HT and BD-HT were compared. DCD hearts were retrieved utilising a direct procurement protocol with NMP. BD hearts were retrieved with either static cold storage (SCS) or hypothermic machine perfusion (HMP).
Results: Over 10yrs, DCD heart transplantation accounted for 22% (110/497) of all heart transplant activity. There was no significant difference in short or long term survival between DCD-HT or BD-HT recipients (5yr survival: 80% vs 78%; 10yr survival: 67% vs 63% respectively, p=0.6) (see figure 1). At 10yrs freedom from CAV following DCD-HT was 58% (not significantly different to BD cohort, p=0.5). There was no significant