Canadian Blood Services

Utilization and Cost of Procurement of Skin, Cardiac and Vascular Allografts and Allograft Products

Industry Analysis and End-User Survey

Final Report 2010

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Introduction

The following report provides a detailing of the utilization and allograft costs for burn treatment, paediatric cardiac surgery, and adult cardiac and vascular surgery in Canada with the exception of Québec. Hospitals in Québec were not included in this project because Québec has an independent tissue system managed by Héma-Québec. The purpose of this project was to determine utilization and cost of procurement within the remaining Canadian jurisdictions.

The report also identifies trends, innovations and technological advances in skin, cardiac and vascular markets that may impact allograft utilization and demand in the 5-10 year horizon.

In order to provide a more complete understanding of utilization and cost of procurement of skin, cardiac and vascular allografts and allograft products in Canada, data and observations from three different sources were reviewed for this report:

1) Market data, product descriptions and market projects from major suppliers;
2) Current academic literature and previous Canadian Council for Donation and Transplantation (CCDT) reports; and
3) A survey of Canadian end-users outside of Québec, including burn centres, paediatric cardiac centres, and adult cardiac and vascular surgical programs.

Skin Allograft Utilization and Cost (2009)

Fourteen (14) Canadian burn programs (outside of Québec) were contacted between January and April 2010. Responses were received from ten (10) programs from British Columbia, Alberta, Saskatchewan, Manitoba, Ontario and Nova Scotia. These programs indicated that there were a total of 131 available burn beds in Canada. Five (5) programs were able to provide detailed utilization data, three (3) programs did not use allograft and two (2) were unable to provide detailed utilization information.

The utilization estimates are detailed in the table *Skin Allograft Utilization (2009)* below. Based on the burn centre survey responses, between 992 and 1,228 patients were treated at a Canadian burn centre. Five (5) burn centres reported using allograft tissue. An average of 5.7 to 7.9% of patients required skin allograft in the five (5) burn centres. The utilization of allograft skin in the five (5) burn centres is estimated to be in the range of 98,850 cm^2 to 135,869 cm^2 in 2009. The utilization from the five (5) burn centres has not been projected to the entire population of burn programs as smaller burn centres in Canada send burn cases requiring skin allograft to larger centres (centres 6 to 8 reported sending cases requiring allograft to one of the larger centres 1 through 5).

The respondents identified that they had received products from the following skin allograft and/or allograft substitute suppliers in 2009:

- Comprehensive Tissue Centre (Edmonton),
- Héma Québec (Saint-Laurent),
- Manitoba Tissue Bank (Winnipeg),
- Regional Tissue Bank (Halifax),
- Community Tissue Services (U.S.),
- Integra Life Sciences (U.S.) / Canada Microsurgical, Inc., and
- LifeCell Corp. (U.S.).

Based on the end-user survey there is a very low reliance on US suppliers of skin allograft at burn centers. The Canadian Blood Services report, *Supply of Human Allograft Tissue in Canada – Final Report 2010,* indicates that 118,300 cm^2 of allograft skin was produced in 2008. As such, it is possible that Canada was self-sufficient in the supply of human allograft skin in 2009.

Skin Allograft Utilization Summary (2009)

1) Burn centre	2) # Beds	3) No. patients per year (low)	4) No. patients per year (high)	5) Average No. patients per year	6) Percentage of patients that require allograft (low) (%)	7) Percentage of patients that require allograft (high) (%)	8) Number of patients that require allograft (low)	9) Number of patients that require allograft (high)	10) Average utilization per patient (cm2)	11) Total Utilization (low) (cm2)	12) Total Utilization (high) (cm2)
1	31	150	225	188	5	8	11	15	3000	32176	44226
2	10	120	140	130	1	2	7	10	3318	24673	33914
3	12	95	95	95	5	10	5	7	1150	6249	8590
4	8	120	120	120	10	10	7	9	5000	34321	47174
5	6	10	15	13	30	30	1	1	2000	1430	1966
6	6	N/A	N/A	N/A	0	0	0	0	0	0	0
7	5	80	80	80	0	0	0	0	0	0	0
8	5	N/A	N/A	N/A	0	0	0	0	0	0	0
Total from Respondents	83	575	675	625			31	43		98850	135869
Average of Respondents (n=67 of 131 beds reporting utilization)					5.7	7.9			3171		

The Skin Allograft Utilization Summary (2009) table above provides the data reported from eight (8) burn centres. The utilization of allograft skin is highly variable between programs. Because of the variation between burn centres weighted averages based on the number of patients treated per year were used to calculate the total utilization estimates. The total number of burn patients per year reported from n=72 burn beds ranged from 575 to 675 patients with an average of 625 patients. Projected to 131 burn beds available in Canada, it is estimated that there are between 992 and 1,228 patients treated at a Canadian burn centre.

Column 1 provides an identification number for each centre. Column 2 shows the number burn beds available at each burn centre. The weighted average for the percentage of patients that required allograft was reported from n=67 of 131 available burn beds.

Column 3, 4 and 5 show the low, high and average number of patients reported to be treated at a burn centre. For the majority of burn centres only a low to high range could be provided for the number of patients treated in 2009.

Column's 6 and 7 show the percentage of patients treated that required allograft skin. As with the total number of patients, most burn centres could only provide a low and high range.

Columns 8 and 9 provide an estimate of the number of patients treated at each burn centre based on the average of the total number of patients at each centre and the average percentage of all centres patients that required allograft (e.g., Centre 1 saw an average of 188 patients in 2009, 5.7 to 7.9% of which required allograft, for a range of 11 to 15 patients). The average percentage of all centres patients requiring allografts was felt to be a more accurate reflection of utilization due to the variation between centres and the variation within centres annually.

Column 10 provides the average utilization of skin allograft per patient (this number was provided by each burn centre).

Columns 11 and 12 provide estimates for the total utilization of skin by each burn centre based on the reported average utilization per patient in column 10 and the estimate of the actual number of patients in columns 8 and 9.

Skin Allograft Cost Summary (2009)

Tissue Type or Product	Estimate Range	No. Patients Treated at a Canadian Burn Centre Requiring Allograft Skin	Allograft Utilization per Patient (cm^2) [Weighted Average of Respondents]	Canadian Utilization of Allograft Skin (cm^2)	Cost from Canadian Tissue Banks * ($Can)	Cost from US Suppliers* ($Can)	Total Cost ($Can)
Frozen Skin Allograft	Low	31 +/- 3	3,171	98,800 +/- 8,300	113,600 +/- 9,500	12,600 +/- 1,000	126,300+/- 10,600
	High	43 +/- 4		135,800 +/- 11,413	156,200 +/- 13,100	17,300 +/- 1,400	173,600 +/- 14,500

*Total cost of allograft is based on an estimate that 92% of the total supply is provided by Canadian tissue banks with the remaining 8% of the total supply is provided by suppliers in the United States[i]. Allograft pricing based on C$1.25/$cm^2$.[ii] Assumed $Can = $US.

Skin Allografts and Allograft Product Trends:

- Surgeons will continue to rely on human allografts until more research and development can produce substitute products with a wider range of applications,
- Demand for fresh and frozen skin is expected to remain the same or decrease in the next 2 to 5 years,
- Cultured autologous keratinocytes are not being used by the respondents to the survey (n=10/10),

- Although the current use of dermal substitutes by Canadian burn centres is small, the majority of respondents indicated that the use of Integra® and other dermal substitutes and advanced wound products would increase in the next two to five years,
- Decreased use of human allograft was reported in smaller Canadian burn centres, and
- A contrast was found between smaller burn centres that do not use allograft and only perform autografting and/or use substitutes like Integra®, and large burn centres that utilize human allograft which is obtained almost exclusively from local Canadian tissue banks.

Paediatric Allograft and Allograft Substitute Heart Valve Utilization and Cost Summary (2009)

All five paediatric cardiac surgical programs in Canada (excluding Québec) were contacted and all provided responses. The cost estimates assume that 70% of paediatric allograft valves are supplied by Canadian tissue banks and 30% are supplied by a US tissue bank (Cryolife[iii]), based on the Canadian Blood Services report, *Supply of Human Allograft Tissue in Canada – Final Report 2010*. Cost estimates for bioprosthetic and mechanical valves are based on the cost of a typical substitute valve (Medtronic Mosaic). Cost for an allograft heart valve is C$6,400 based on list pricing from RTB Halifax[iv] and CTC Edmonton. Cost for a <23mm pulmonary valve with or without conduit, and a 17mm aortic valve from Cryolife is $9,995 (assumed $Can = $US).

The utilization of cardiac valve allograft in the paediatric population is estimated to be in the range of 94 +/-11 valves, with 90% being pulmonary valves and 10% aortic.

The respondents identified that they had received paediatric cardiac valves from the following suppliers in 2009:

- Comprehensive Tissue Centre (Edmonton),
- The Hospital for Sick Children (Toronto),
- Regional Tissue Bank (Halifax), and
- Cryolife (U.S.).

Paediatric Heart Valve Utilization Summary (2009)

	Centre 1	**Centre 2**	**Centre 3**	**Centre 4**	**Centre 5**	**Total [+/-] or Average %**
Total number of valve replacements per year	83 to 97	50 to 75	50	10	35	**248 +/-20**
Utilization of allograft (% of all valve replacement procedures)	20%	80 to 90%	20%	50%	30%	**40%**
Actual number of allografts used	**17 to 19**	**40 to 60**	**10**	**5**	**11**	**94 +/-11**
Utilization of bioprosthetic Valves or conduit (% of all valve replacement procedures)	50%	10%	60%	30%	50%	**40%**
Utilization of mechanical valves (% of all valve replacement procedures)	30%	10%	20%	20%	20%	**20%**
Percentage of total procedures where allograft is preferred but not available	50%	5%	40%	80%	60%	**50%**
Number of additional valve replacements that would have used allograft if available	**42 to 48**	**3 to 4**	**20**	**8**	**21**	**97 +/-4**

Paediatric Heart Valves Cost Summary (2009)

Tissue Type or Product	Utilization as a Percentage of Total Valve Replacement Procedures	Allograft or Substitute Type	Canadian Valve Utilization (No. valves)	Cost ($Can) from Canadian Tissue Banks	Cost ($Can) from US Suppliers	Total Cost ($Can)
Paediatric Allograft Heart Valves	40%	90% pulmonary 10% aortic	94 +/-11	421,120 +/- 49,280	281,859 +/- 32,984	702,979 +/- 82,264
Paediatric Bioprosthetic Valves	40%	90% pulmonary 10% aortic	94 +/- 11		612,786 +/- 71,696	612,786 +/- 71,696
Paediatric Mechanical Heart Valves	20%	90% pulmonary 10% aortic	47 +/- 5		306,393 +/- 35,848	306,393 +/- 35,848

It may be assumed that if an allograft is not available in Canada then it can be supplied by suppliers in the US (e.g., Cryolife). However, due to high costs and the limited availability of smaller valve sizes, this is not the case and an alternative bioprosthetic or mechanical valve must be used even though allograft is preferred in the vast majority of cases for paediatric patients. In future studies it may be worthwhile to calculate the opportunity cost of having to purchase bioprosthetic valves or allograft valves from the U.S. versus investing in increasing Canadian production capability.

Paediatric Cardiac Valve Replacement Trends:

- Much higher percentage of human allograft heart valves used in paediatric surgery at approximately 40% of all valve related procedures vs. 1.67 % for adults,

- 4 of 5 paediatric surgical program medical directors stated that they had to use alternatives to human allograft an average of 57% of the time due to the limited availability of human allografts. Only one (Centre 2 in the table above) was able to use human allograft 95% of the time due to proximity to a tissue bank,
- Highest demand (~90%) is for pulmonary valves, with 15-17 mm and <15 mm sizes noted as extremely difficult to obtain,
- The majority of paediatric cardiac end-users surveyed believe demand for allografts and allograft products will stay the same in the next 5 years with possible increases in bioprosthetic valves and decellularized valves as the technology emerges,
- Improvements in catheter-based surgeries that are allowing more minimally invasive valve implantation which may delay the need for re-operation,
- In the long-term, stem cell research seems to have the potential to address some critical requirements for paediatric heart valves but this technology will not effect utilization in the next 10 years, and
- Paediatric cardiac end-users depend heavily on suppliers in the United States for allograft, bioprosthetic and mechanical valves.

Adult Allograft Heart Valve Utilization and Cost (2009)

Seventy-six (76) cardiac surgeons were identified at twenty-three (23) Canadian hospitals for the survey. The department head or program medical director and administrative manager for each hospital were contacted. Nine (9) hospitals responded to the survey including hospitals from British Columbia, Alberta, Manitoba, Ontario and Nova Scotia. Forty-six (46) of the 76 surgeons were represented in the nine responses providing a confidence interval of +/- 9.1 % at a 95% confidence level for the data provided in the table above.

The utilization of cardiac valve allograft in the adult population is estimated to in the range of 65 +/-12 valves.

The cost estimates assume that 70% of allograft valves are supplied by Canadian tissue banks and 30% are supplied by a US tissue bank (Cryolife)[v]. Cost estimates for bioprosthetic and mechanical valves are based on the cost of a typical substitute valve (Medtronic Mosaic). Cost for an allograft heart valve is C$6,400 based on list pricing from RTB Halifax and CTC Edmonton. Cost for a 23mm pulmonary valve with or without conduit, and a 25mm aortic valve from Cryolife is $11,545 (at par).

The respondents identified that they had received cardiac valves from the following suppliers in 2009:

- Comprehensive Tissue Centre (Edmonton),
- The Hospital for Sick Children (Toronto),
- Regional Tissue Bank (Halifax), and
- Cryolife (U.S.).

Adult Allograft Heart Valve Utilization and Cost Summary (2009)

Data Source	Annual Number of Valve Replacement Procedures	Percentage of Valve Replacement Procedures Using Allograft Tissue[vi]	Canadian Utilization Annual Estimate	Estimated Cost ($Can)		
				Canadian Supply	US Supply	Total
Projected from end-user survey	3,821 +/- 349	1.67 % +/- 0.15	65+/-12	291,200 +/- 53,760	225,128 +/- 41,562	516,328 +/- 95,322

Adult Cardiac Valve Replacement Trends

- A small percentage of human allograft heart valves are used in adult valve replacement procedures (1.67% +/- 0.15),
- The respondents stated that they had to use alternatives to human allograft less than 10% of the time due to the limited availability of human allografts,
- The majority of cardiac end-users surveyed believe demand for allografts and allograft products will stay the same in the next 5 years (with possible slight increases in bioprosthetic valves and decellularized valves as the technology emerges),
- Cardiac end-users dependence on suppliers in the United States for allograft heart valves is low due to the low number of adult procedures that use allograft, as a percentage of procedures (approximately 20 valves).
- The valves used in adult procedures were reported to be utilized in the following ranges: 70% to 75% of all valve replacements are bioprosthetic; 20 to 29% are mechanical valves; 0 to 5% are allograft,
- Increased development of transcatheter technologies for minimally invasive heart valve transplants,

- Continued need for patients that have an infected mechanical or bioprosthetic valve to require valve replacement surgery using human tissue grafts. Infected valves are reported as occurring in 1 to 6% of all prosthetic vascular procedures, and
- Continued research in to reducing degeneration and calcification (particularly by Cryolife).

Adult Vascular Allograft Utilization Summary

The response obtained from vascular and cardiothoracic surgeons could not provide an accurate picture of vascular allograft tissue utilization in Canada (38 of 216 vascular and cardiothoracic surgeons). While nine (9) vascular programs from across Canada did respond to the survey none utilized human allograft tissue in 2009.

Since it is known that Canadian Tissue Banks distribute some vascular allografts, a request was made to the Canadian Institute for Health Information (CIHI) for data on the frequency of cardiac and vascular cases that utilize allograft (e.g. valves, arteries and veins). The Discharge Abstract Database (DAD) was accessed for acute care cases from April 1, 2008 to March 31, 2009 for the number of procedures performed outside of Québec, for all age groups.

One hundred and eighty-eight (188) procedure code classifications from the 2006 Canadian Classification of Health Interventions (CCHI) were identified that could use allograft cardiac and vascular tissue. There were a total of two hundred and eighty (280) acute care cases that utilized allograft cardiac and/or vascular tissue. Of these, twenty-five (25) procedure code classifications utilize allograft heart valves for valve replacement or repair procedures, and two (2) utilize allograft valves as part of major aortic arch repair. One hundred and twenty-eight (128) acute care cases utilizing an estimated 158 allograft heart valves were identified.[vii]

Of the 161 other procedure code classification that can utilize allograft vascular tissue, there was a total of one hundred and fifty-two (152) acute care cases that utilized allograft vascular tissue.

The table Adult Vascular Allograft Utilization (2008/09) provides a summary of the procedure groups and frequency for the procedures that utilized allograft tissue.

Adult Vascular Allograft Utilization (2008/09)

Procedure Type	Case Frequency (Annual)	Percent of Cases
Extraction, bypass or repair abdominal arteries and aorta (not utilizing valves)	83	54.6%
Excision or extraction carotid artery	22	14.5%
Division, repair or excision of pulmonary arteries	17	11.2%
Extraction or repair of arteries of leg	10	6.6%
Bypass, repair or excision vena cava	5	3.3%
Other	5	3.3%
Extraction, bypass or repair brachiocephalic arteries	4	2.6%
Repair, arteries of arm	4	2.6%
Extraction or repair of coronary arteries	2	1.3%
Division, repair or excision of pulmonary vein	0	0.0%
Extraction or repair subclavian artery	0	0.0%
Extraction or repair mammary artery	0	0.0%
Total	**152**	100%

The Canadian Blood Services report, *Supply of Human Allograft Tissue in Canada – Final Report 2010*, indicates that 185 cardiovascular grafts were distributed in 2008, including 111 heart valves, and 74 non-valve of cardio-vascular grafts (veins and arteries). CIHI reports 152 non-valve allografts utilized in 2008.

Based on the Canadian Blood Services report, *Supply of Human Allograft Tissue in Canada – Final Report 2010* and the data obtained from CIHI, there was a shortfall of 79 non-valve cardiovascular allografts in 2008.If the shortfall of vein and arterial grafts is being purchased from the US, an in particular from CryoLife, this could be a significant cost area (e.g., CryoLife charges between US$3-4,000 for vein and arterial grafts.

[i] Canadian Council for Donation and Transplantation. Human Tissue Importation Practices in Canada, October 2006. This estimate for Canadian and US skin utilization are used as survey respondents did not provide comprehensive purchasing information.
[ii] Comprehensive Tissue Centre, Alberta Health Services, Tissue Allograft Catalogue, February 2010.
[iii] Canadian Blood Services, Supply of Human Allograft Tissue in Canada – Final Report 2010. 2008 Canadian production was aligned to estimated utilization to estimate percentage of importation.
[iv] Halifax Regional Tissue Bank Fee Schedule. December 2008.
[v] Canadian Blood Services, Supply of Human Allograft Tissue in Canada – Final Report 2010. Canadian production was aligned to estimated utilization to estimate percentage of importation.
[vi] Allograft type included 56.9% single aortic valve replacement, 19.6 % single mitral valve replacement, 17.7% dual valve replacement and 5.8% triple valve replacement based on data from the British Columbia Medical Services Plan data for 2009.
[vii] Based on data obtained from the British Columbia Medical Services Plan (MSP) database, 76.5% of valve replacement procedures utilize single valves, 17.7% utilize two valves and 5.8% utilize three valves. For the DAD data above, based on the BC MSP utilization 114 homograft valve procedures could have utilized up to 158 homograft valves (98 single valves replacements, 45 double and 15 triple). Based on the end-user surveys, 159 +/-12 homograft valves were utilized in 2009 for all age groups.