Are Allografts Better than They Used to Be?

February 3, 2018

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Disclosures

- Utter : None

History

1881	1st allograft, tibia from rickets osteotomy to treat humeral osteomyelitis
1950	Navy Tissue Bank in Bethesda Maryland, freeze dried preservation
1963	Gamma radiation of allograft
1984	First case of AIDS transmitted via allograft
1987	CDC guidelines published for donor testing
1991	ELISA for AIDS testing
2005	PCR testing for HIV & HCV
2010	Glycerol preservation

Infection

Testing	Prevalence among donors
Anti-HIV	0.093%
HBsAg	0.022%
Anti-HCV	1.091%
Anti-HTLV	0.068%

- *Treponema pallidum*
- Human transmissible spongiform encephalopathies
- *Clostridium spp.* or *Streptococcus pyogenes* cultures, bacterial infection estimated 1/100,000-1/200,000

Buck et al, *Clin Orthop Relat Res* 1994, 8-17
Zou et al. *NEJM* 2004, 351:75-9

Processing

- Aseptic harvesting & handling
- Freeze drying, Fresh Frozen, Glycerol
- Wash: Multiple antibiotics, H_20_2, acetone, hyperosmotic saline, ethanol, ethelene oxide, ultrasonic baths
- Gamma irradiation, 25kGy, "low dose"
- Pretreatment with radioprotectant scavengers to help maintain structural integrity.

Table 2
Comparison between aseptic processing, ethylene oxide, gamma irradiation, and chemical soaking methods and their sterilization abilities and properties[16]

	Aseptic Processing	Ethylene Oxide	Gamma Irradiation	Chemical Soaking
Kills bacteria	No	Yes	Yes	Yes
Kills fungi	No	Yes	Yes	Yes
Kills spores	No	Yes	Yes	No
Kills enveloped and non-enveloped viruses (eg, HIV, hepatitis A)	No	Yes	Yes (dose-dependent)	No
Removes blood and lipids	Surface only	No	No	Surface only
Preserves strength	Yes	Yes	Decreases (dose-dependent)	Yes
Preserves biocompatibility	Yes	Yes	Yes	Yes
Penetrates into tissue	Surface only	Thickness-dependent	Full penetration	Surface only

Vangsness et al. *Arthroscopy* 2006; 22(12): 1351-8

Table 3
Specific sterilization methods used by specific tissue banks

Tissue Bank	Nonprofit, for Profit	Sterilization Method
rti surgical	For profit	BioCleanse—A validated, automated, pharmaceutical sterilization process using vacuum/pressure and chemical sterilants. The Tutoplast process comprises numerous phases as shown in the following example: 1. Lipids are removed in an ultrasonic acetone bath. 2. A series of alternating hyperosmotic saline and deionized water baths. 3. An oxidative treatment with hydrogen peroxide (H_2O_2). 4. A final acetone wash. The acetone wash, followed by vacuum extraction, dehydrates the tissue. Terminally sterilized using low-dose gamma irradiation. Yields a SAL of 10^{-6}.
LifeNet Health	Nonprofit	Allowash XG (An intensive decontamination and scrubbing regime) gamma irradiated, sterility validated. Validated to SAL of 10^{-6}.

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Table 3
Specific sterilization methods used by specific tissue banks

mtfbiologics	Nonprofit	Allograft tissue purification process (ATP)
Community Tissue Services	Nonprofit	Grafts are soaked and rinsed in antibiotics, hydrogen peroxide, alcohol, sterile water, and Allowash solutions and irradiated at a dosage between 15 and –25 kGy.
Osteotech	For profit	Permeint TM Combination of ethanol and nonionic detergent.
BONE BANK ALLOGRAFTS	Nonprofit	GraftCleanse- ISO 11,137-2 Method-1 A validated sterilization process with an SAL of 10^{-6} gamma sterilized at 19.8–24.2 kGy.
AlloSource	Nonprofit	Validated SterileR disinfection process plus low-dose gamma irradiation assures SAL of 10^{-6}.
TISSUE BANKS INTERNATIONAL	Nonprofit	TranZgraft Proprietary wash plus low-temperature, low-dose gamma irradiation. A validated sterilization process with an SAL of 10^{-6}.

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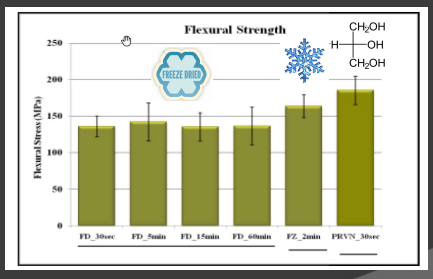
Allograft Biomechanics & Preservation Methods



Sohini et al. ORS Annual Meeting 2011

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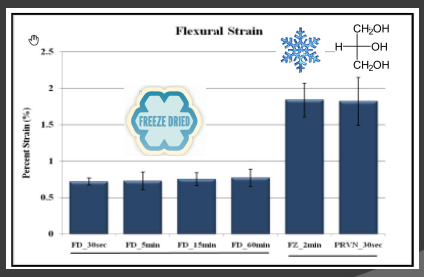
Allograft Biomechanics & Preservation Methods



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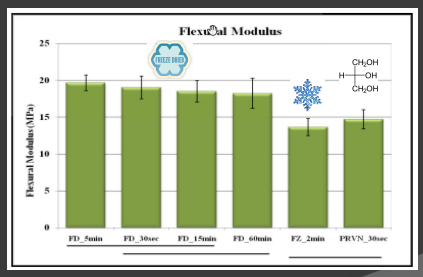

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Fusion Studies

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A Prospective, Randomized, Blinded, Single-Site Study to Evaluate the Clinical and Radiographic Differences Between Frozen and Freeze-Dried Allograft When Used as Part of a Circumferential Anterior Lumbar Interbody Fusion Procedure

- No difference in complications overall
- More implant fractures during insertion for freeze dried (12) vs. frozen (4)
- More pseudoarthosis in freeze dried vs. frozen (p=0.026)
- Better clinical outcomes in frozen vs. freeze dried

Thalgott et al. Spine 34(12):1251-6, 2009

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Evaluation of glycerol-preserved bone allografts in cervical spine fusion: a prospective, randomized controlled trial

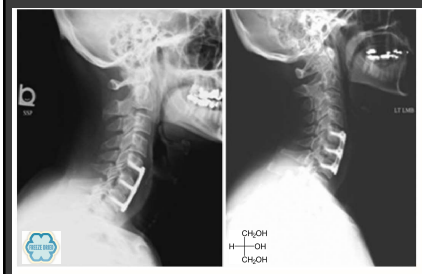

FIG. 3. Representative radiographs of freeze-dried **(left)** and glycerol-preserved **(right)** grafts at the 6-month follow-up show fusion in both treatment groups.

n = 106 patients

53 freeze dried vs
53 glycerol preserved
Cloward dowels

Primary endpoints:
Subsidence
Fusion
Secondary endpoint:
Adverse events

Graham et al. JNS Spine 2015; 22:1-10

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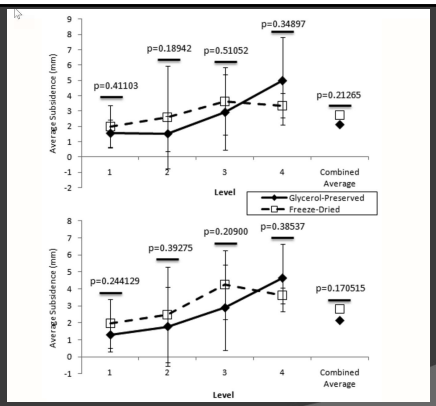

Graham et al. JNS Spine 2015; 22:1-10

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TABLE 2. Summary of all adverse events recorded in the course of the study

Adverse Event	No. of Cases (%)	
	Glycerol-Preserved Graft	Freeze-Dried Graft
Severe event, possibly graft related*		
Neck pain	1 (0.9)	0
Segmental kyphosis level below the fusion	0	1 (0.9)
Deep wound infection	0	1 (0.9)
Subtotal	1 (0.9)	2 (1.8)
Mild–moderate event, possibly graft related*		
Neck pain	1 (0.9)	0
Neck & shoulder pain	0	1 (0.9)
Arm pain	1 (0.9)	0
Subsidence	2 (1.8)	2 (1.8)
Persistent movement of lowest level on flexion/extension	1 (0.9)	0
Pseudofusion of lowest level of 3-level anterior cervical fusion	0	1 (0.9)
Subtotal	5 (4.6)	4 (3.7)
Event, not graft related*		
Neck pain	6 (5.6)	6 (5.6)
Dysphagia	3 (2.8)	4 (3.7)
Neck & shoulder pain	6 (5.6)	1 (0.9)
Neck & arm pain	2 (1.8)	4 (3.7)
Back pain	2 (1.8)	3 (2.8)
Arm pain	0	3 (2.8)
Shoulder pain	2 (1.8)	1 (0.9)
Radiculopathy	1 (0.9)	2 (1.8)
Hand numbness	2 (1.8)	0 (0)
Miscellaneous (1 occurrence each)	19 (17.6)	29 (26.8)
Subtotal	43 (39.8)	53 (49.1)

* As assessed by the Data Safety Monitoring Board or examining physician.

Graham et al. JNS Spine 2015; 22:1-10

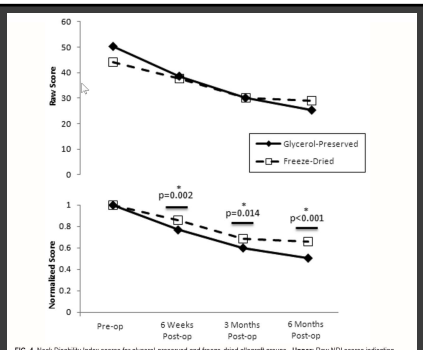


FIG. 4. Neck Disability Index scores for glycerol-preserved and freeze-dried allograft groups. **Upper:** Raw NDI scores indicating a trend toward lower postoperative scores for both treatment groups. **Lower:** Raw NDI scores normalized to prescreening scores. The normalized scores showed statistically significant improvement in NDI scores at every follow-up time point in the glycerol-preserved group over the freeze-dried group. *Asterisk* indicates statistical significance toward a lower NDI score with glycerol-preserved allografts.

Graham et al. JNS Spine 2015; 22:1-10

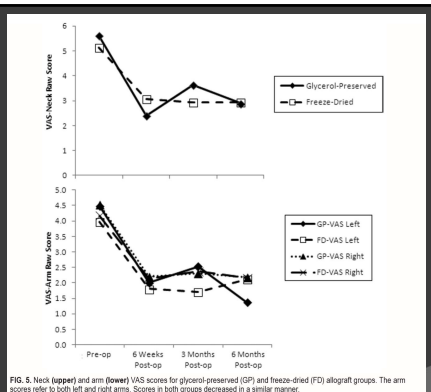
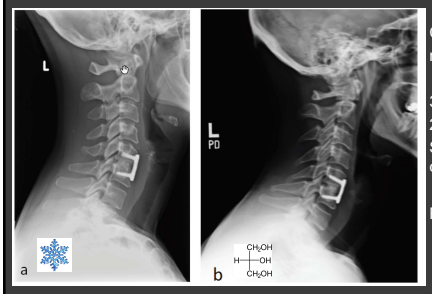


FIG. 5. Neck **(upper)** and arm **(lower)** VAS scores for glycerol-preserved (GP) and freeze-dried (FD) allograft groups. The arm scores refer to both left and right arms. Scores in both groups decreased in a similar manner.

Graham et al. JNS Spine 2015; 22:1-10

Comparison of Fusion Rates between Glycerol-Preserved and Frozen Composite Allografts in Cervical Fusion



Consecutive cohort
n = 67 patients

37 frozen vs
28 glycerol preserved
Smith Robinson,
composite allograft

Primary endpoints:
Fusion at 3 mo
Fusion at 1 yr

Rodway and Gander, *International Scholarly Research Notices* 2014
http://dx.doi.org/10.1155/2014/960142

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Comparison of Fusion Rates between Glycerol-Preserved and Frozen Composite Allografts in Cervical Fusion

	Frozen				Glycerol-preserved				
	Total patients	Fused grafts	Not fused	% of fused patients	Total patients	Fused grafts	Not fused	% of fused patients	Frozen versus glycerol statistically similar?
Three months	38	16	22	42.1%	29	11	18	37.9%	Yes ($P = 0.7343$)
12 months	24.5	24.5	0	100%	17.5	17.5	0	100%	Yes ($P > 0.999$)

*Note that 2 patients had both glycerol-preserved and frozen grafts 1 level for each type. The results from those patients were counted as 1/2 patients in each group.

Rodway and Gander, *International Scholarly Research Notices* 2014
http://dx.doi.org/10.1155/2014/960142

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Conclusions
Are Allografts better than they used to be?

Yes, in small incremental improvements:

- Better detection of infection (>1990)
- Better preparation techniques (>2000)
- Improved biomechanical properties (>2010)
- Fusion improvement
- Cost improvement

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Thank You!

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