

# Promises and Perils of Using an Innovation Paradigm for the Clinical Translation of Stem Cell Research

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# Disclosures

- I serve on the Bioethics Advisory Panel and the Stem Cell Research Oversight Committee for Merck KGaA
- I receive consulting income for these activities





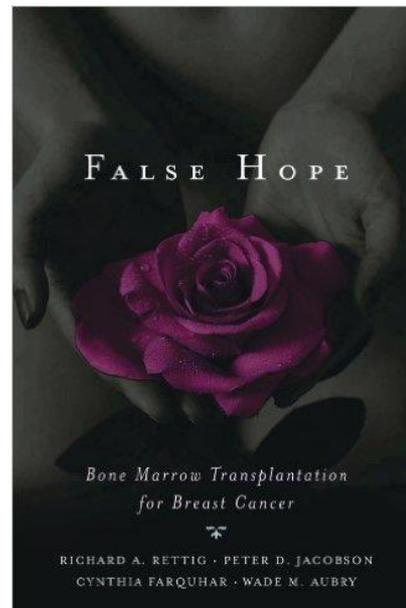


# Selected Conditions Treated

- Cancers
  - ALL, AML, CML
- Bone marrow failure syndromes
  - Aplastic anemia, Fanconi's
- Hemoglobinopathies
  - Sickle cell, thalassemia
- Inborn errors
  - SCID

# HDCT/ABMT or Breast Cancer

- Rapid dissemination of an innovative therapy offering hope
- >30,000 women received it before it was shown to be ineffective



# THE LANCET

The Lancet, Early Online Publication, 23 October 2013  
doi:10.1016/S0140-6736(13)62033-4

## Groundbreaking Trachea Transplant Could Become Routine

Oct. 23, 2013

By KATIE MOISSE via [GOOD MORNING AMERICA](#)

*Science* 19 April 2013:  
Vol. 340 no. 6130 pp. 266-268  
DOI: 10.1126/science.340.6130.266

NEWS FOCUS

### Trachea Transplants Test the Limits

## Help Hannah Breathe



**\$50,000** of \$50,000

100%

**609** donations

**0** days left

Fundraiser ended on  
**August 22nd, 2013**

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# Girl Dies After Groundbreaking Trachea Transplant

July 8, 2013

By KATIE MOISSE via **WORLD NEWS**

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  30 Comments 









stem cell treatments



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About 25,300,000 results (0.25 seconds)

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Over 8 Years Experience · Minimally Invasive & Safe · Free Candidate Evaluation  
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### Non-Surgical Alternatives - stemcellarts.com

Ad [www.stemcellarts.com/](http://www.stemcellarts.com/)

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### Stem Cell Therapy - Advanced Stem Cell Treatments

Ad [www.worldstemcellinstitute.org/](http://www.worldstemcellinstitute.org/)

Contact Us For Help Today!

### Scholarly articles for stem cell treatments

... **stem cell** transplantation and **cell** therapy as an ... - **Slavin** - Cited by 2102  
**Treatment** of severe acute graft-versus-host disease ... - **Le Blanc** - Cited by 2216  
... mesenchymal **stem cell** infusion for **treatment** of ... - **Koc** - Cited by 660

Ads

### Stem Cell 100 on Amazon

[www.amazon.com/](http://www.amazon.com/)

4.4 ★★★★★ rating for amazon.com  
Turn Back the Clock on Aging,  
Look and Feel Younger!

### New Stem Cell Treatments

[www.stemcellofamerica.com/stem-cell](http://www.stemcellofamerica.com/stem-cell)

Cutting Edge **Stem Cell** Procedures  
Painless Procedure, Takes One Hour!

### Stem Cell Therapy Plus

[www.stemcelltherapyplus.com/](http://www.stemcelltherapyplus.com/)

(302) 483-7786  
**Stem Cell Therapy** Switzerland  
For Degenerative Diseases.

### Stem Cell Therapy

[www.dermamed.com.au/](http://www.dermamed.com.au/)

**Table 1. Nature of Therapies Offered across Surveyed Websites**

Stem Cell Type	Frequency	%
Adult, autologous	9	47
Fetal	6	32
Cord blood	4	21
Embryonic	2	11
Adult, allogeneic	2	11
Adjuncts	0	0
Unspecified	0	0
Stem Cell Source	Frequency	%
Bone marrow	7	37
Blood or marrow donors	5	26
Peripheral blood	5	26
Fetuses	4	21
Fat	2	11
Unspecified	2	11
Other	3	16
Transplantation Procedure	Frequency	%
Intrathecal, into the CSF	6	32
Intravenous	6	32
Subcutaneous or intramuscular	4	21
Surgical transplantation	4	21
Catheterization of deep body vessels	3	16
By mouth	1	5
Topical	1	5

**Table 1 Demographics of patient undergoing stem cell treatment as reported in news media articles from October 2006 to September 2009**

<b>Gender</b>	<b>Age (adult versus minor)</b>	<b>Country of origin (in descending order)</b>	<b>Five most common conditions</b>	<b>Three most common treatment destinations</b>
Male (134; 59.8%)	Adult (126; 56.3%)	US (84; 37.5%)	Multiple sclerosis (22; 9.8%)	China (100; 44.6%)
Female (87; 38.8%)	Minors (98; 43.8%)	UK (80; 35.7%)	Cerebral palsy (18; 8.0%)	Germany (17; 7.6%)
Unspecified (3; 1.3%)		Australia (32; 14.3%)	Septo-optic dysplasia (15; 6.7%)	Mexico (17; 7.6%)
		Canada (12; 5.4%)	Optic nerve hypoplasia (13; 5.8%)	
		New Zealand (12; 5.4%)	Unspecified blindness (13; 5.8%)	
		Israel (1; 0.5%)		
		Brazil (1; 0.5%)		

Zarreczny, et al. *Nature Biotechnology*, 2010

# ISSCR Guidelines

- Cell processing and manufacturing
- Pre-clinical studies
- Clinical research
- Medical innovation
- Social justice

# ISSCR

## Stem Cell-Based Medical Innovation

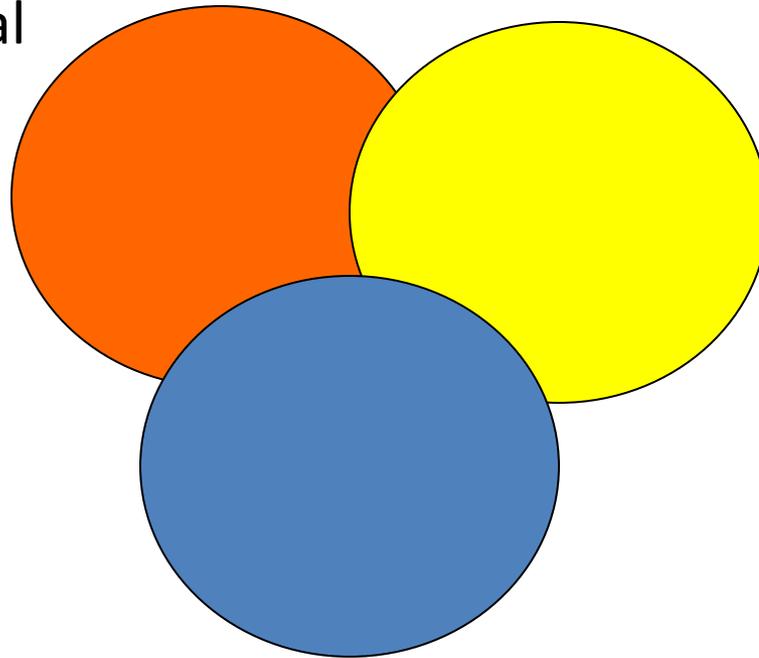
“Clinician-scientists may provide unproven stem cell-based interventions to at most a very small number of patients outside the context of a formal trial, provided...”

# Acceptable Stem Cell-Based Medical Innovation: Provisions

- There is a written plan
- Plan is approved through peer review
- Institution is accountable
- Personnel are qualified
- Voluntary informed consent
- Action plan for adverse events
- Resources for complications
- Commitment to contribute to generalizable knowledge

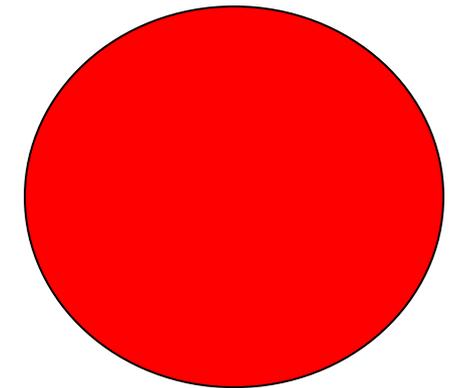
# Clinical Pathways

Translational  
Research



Innovation

Clinical Care



Inappropriate Use

# Conceptual Issues

- Definitions
  - Variation
  - Innovation
- Towards a conceptual model
- Approaches to oversight

# Variation

“the minor modification of a surgical procedure that does not have the reasonable expectation of increasing risk to the patient.”

Biffi, 2008

# Innovation

“a new or modified surgical procedure that differs from currently accepted local practice, the outcomes of which have not been described, and which entail risk to the patient. Many innovations are used on an *ad hoc* basis as dictated by the clinical situation. Some innovations, however, may be developed in a more systematic fashion and may ultimately meet the criteria for human subjects research, although they do not meet the criteria at the time they are developed.”

Biffl, 2008

# Surgical Innovation

“an intervention that is not yet viewed by the institution, community, or profession as meeting the accepted standards of safety, reliability, and familiarity (on the part of patients and the health care team) with effects, side effects, and complications.”

– McKneally and Daar

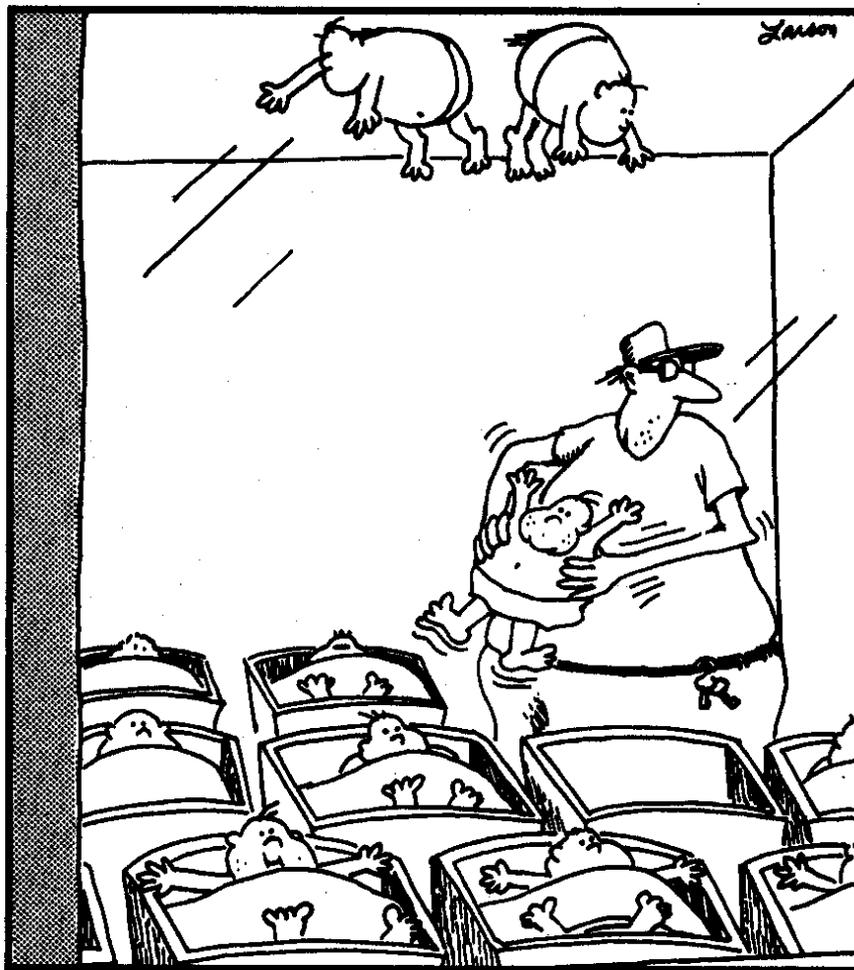
# The Lens of Research

## Belmont Report

“When a clinician departs in a significant way from standard or accepted practice, the innovation does not, in and of itself, constitute research. The fact that a procedure is "experimental," in the sense of new, untested or different, does not automatically place it in the category of research. Radically new procedures of this description should, however, be made the object of formal research at an early stage in order to determine whether they are safe and effective. Thus, it is the responsibility of medical practice committees, for example, to insist that a major innovation be incorporated into a formal research project.”

# Towards a Conceptual Model

- A real prospect of benefit to the patient
- Fiduciary nature of the clinician-patient relationship
- Minimal incremental risk
- Humility
- Transitory phase to research or abandoning the approach
- Responsibility for balanced dissemination of information
  - Reports
  - Registries
  - Clinical trials



Late at night, and without permission, Reuben would often enter the nursery and conduct experiments in static electricity.

# Common Features of Approaches to Oversight of Innovation

- A recognition that innovation can be harmful
- A need for oversight
  - Appropriate expertise
  - Appropriately burdensome
- Patient consent
- An acknowledgement of conflicts
- Reporting

# Closing Comments

- Innovation has resulted in enormous benefits and enormous harms
- Approaches to 'responsible innovation' share some common features
- There is a clear need for conceptual work addressing the notion of innovation
- This conceptual work would be enhanced with a prospective empirical mapping of approaches to innovation