

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





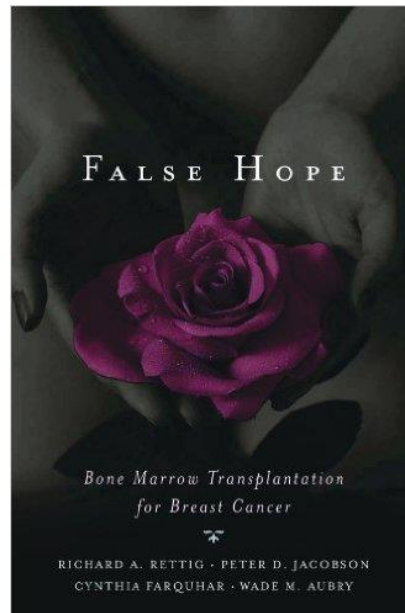


Selected Conditions Treated

- 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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stem cell treatments



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Ads

Stem Cell 100 on Amazon

www.amazon.com/
4.4 ★★★★★ rating for amazon.com
Turn Back the Clock on Aging,
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Stem Cell Therapy Plus

www.stemcelltherapyplus.com/
(302) 483-7786
Stem Cell Therapy Switzerland
For Degenerative Diseases.

Stem Cell Therapy

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

Gender	Age (adult versus minor)	Country of origin (in descending order)	Five most common conditions	Three most common treatment destinations
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

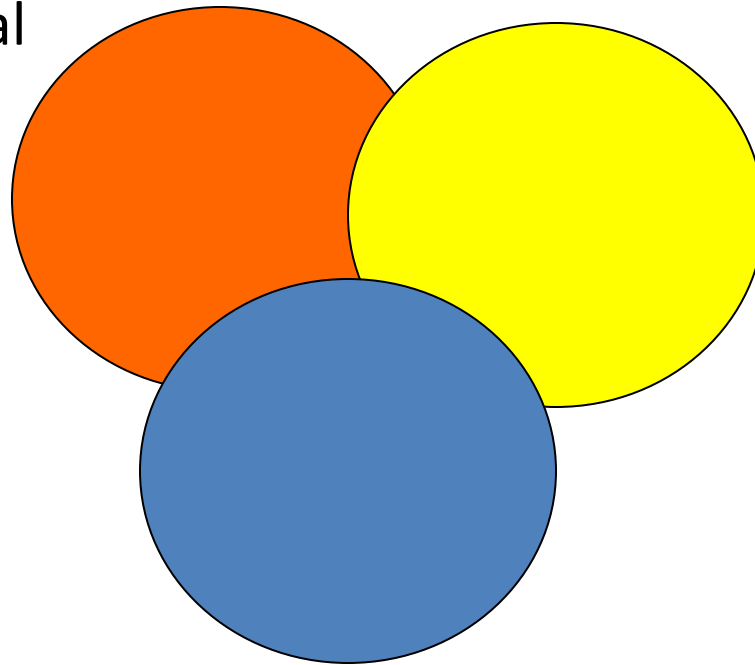
“Clinician-scientists may provide unproven stem cell-based interventions to at most a very small number of patients outside the context of a formal trial, provided...”

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

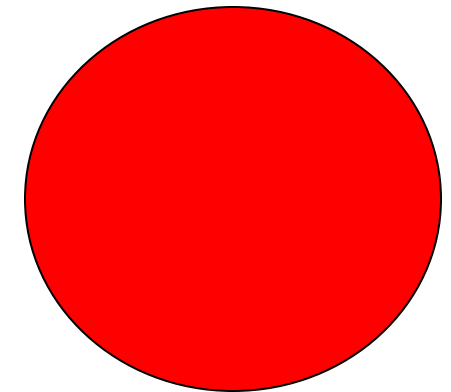
Clinical Pathways

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.”

Biffi, 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

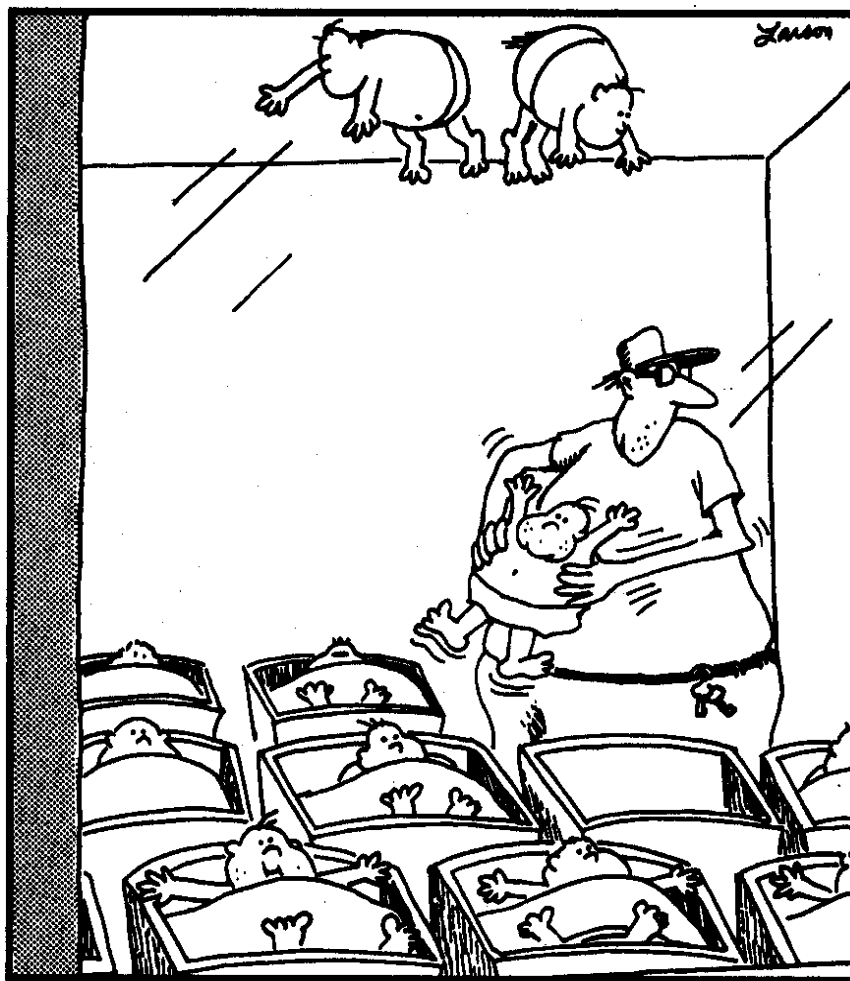
The Lens of Research

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