KIPP A. VAN CAMP, DO

CLASS OF 1990 UHS/KCUMB

DIAGNOSTIC AND INTERVENTIONAL RADIOLOGY

Brief Stem Cell History

- 1868 Term "stem cell" appears in scientific literature, German biologist Ernst Haeckel describes a fertilized egg that becomes an organism as a stem cell
- 1886 William Sedgwick uses term "stem cell" to describe parts of a plant that grow and regenerate
- 1909 Russian Alexander Maximow introduces the theory (at the Berlin Hematological Society) that all blood cells come from the same ancestor cell, are multi-potent (have the ability to differentiate into several types of cells.)
- 1953 Maine, USA scientist, Leroy Stevens doing cancer research on mice find scrotal tumors known as teratomas (mixture of differentiated and undifferentiated cells.) He concluded these cells were pluripotent, meaning they could differentiate into any cell found in a fully grown animal.

Brief Stem Cell History

- 1957 Donnall Thomas, physician scientist in Seattle Washington, USA, attempts first human bone marrow transplantation (later winning Nobel Prize in Medicine in 1990 for his work).
- 1968 Robert Good, U of Minn, US physician performs first successful bone marrow transplant on a child with a familial immune deficiency. BM from his sister…both children grew into young adulthood.
- 1981 Two scientists, Martin Evans (Univ of Cambridge) and Gail Martin (Univ of CA) conducting separate studies derive pluripotent stem cells from the embryo of mice. These are the first embryonic stem cells ever to be isolated.

Brief Stem Cell History

- 1986 Andrew Lasser and Harold Weintraub of Seattle Washington, USA in a scientific experiment, successfully convert a rodent fibroblast (a type of connective tissue cell) into a myoblast (which generates muscle cells).
- 1989 Group of three scientists (Mario Capecchi, Martin Evans, and Oliver Smithies) create the first "knockout mice" which are bred in the laboratory to be missing specific genes. These mice are created using embryonic stem cells.
- 1998 Team from Univ of Wisc create the first batch of human embryonic stem cells which were derived from early embryos. These stem cells are confirmed to be pluripotent

Regenerative Medicine

- The term "regenerative medicine" was first found in a 1992 article on hospital administration by Leland Kaiser. Kaiser's paper closes with a series of short paragraphs on future technologies that will impact hospitals. One paragraph had "Regenerative Medicine" as a bold print title and stated, "A new branch of medicine will develop that attempts to change the course of chronic disease and in many instances will regenerate tired and failing organ systems."

What is Regenerative Medicine

- **Regenerative medicine** is a branch of translational research in tissue engineering and molecular biology which deals with the "process of replacing, engineering or regenerating human cells, tissues or organs to restore or establish normal function".

- This field holds the promise of engineering damaged tissues and organs via stimulating the body's own repair mechanisms to functionally heal previously irreparable tissues or organs.

What are Stem Cells?

- Stem cells are human cells that have the potential to develop into other cell types within the body and thereby repair injured cells.
- All stem cells have three gene properties:
  - Divide and renew themselves.
  - They are unspecialized; they do NOT belong to any specific tissue structure which would allow them to perform a specialized function (such as pumping blood through the body).
  - Although they are unspecialized, they may develop into specialized cells through a process of differentiation.

Types of Stem Cells

- Totipotent
  - These are the stem cells that have the full ability to develop into ALL of the other cells within the body. They are present at fertilization, and are present for 4 days immediately following conception, at which point they then become pluripotent.

- Pluripotent
  - Pluripotent stem cells can develop into any type of cell in the body, except for the cells necessary for fetal development. Generally, pluripotent stem cells are taken from embryos that are a few days old, or are derived from fetal tissue obtained from terminated pregnancies.

- Multipotent
  - These stem cells can only develop into cells with the same tissue of origin; blood stem cells can develop into other blood cells, but not into, say, brain cells.

Sources of Stem Cells

- Three Sources:
  - Embryonic
    - These stem cells come from fetal tissue. They are pluripotent. These cells form within the blastocyst of the developing embroyo. When these cells are removed, the embryo dies. If extracted within the first 4-5 days after fertilization, before these cells begin to differentiate, they can be maintained in the laboratory as undifferentiated embryonic stem cells to creat an embryonic stem cell line.
  - Adult Origin
    - Adult stem cells are found within the tissue of the human body after birth. These cells can renew themselves and can differentiate to generate the specialized cell type of the tissue from which the cell derives in order to replace cells that are lost, diseased, or damaged. They have reportedly been found in the placenta, umbilical cord blood, brain, bone marrow, blood vessels, skeletal muscle, skin and liver. It was thought these cells were multipotent and could only develop into the same tissue. However, recent studies show these cells have demonstrated pluripotent properties suggesting that they can differentiate into different tissue.
  - Newborn Origin
    - Same stem cells as "adult stem cells" but from the Newborn

Nomenclature

Autologous Stem Cells

- Harvested from a persons own source of cells…their own fat, bone marrow, blood

Adult Harvested Stem Cells

- From any human after they are born
  - Newborn from Cord Blood (allogenic)
  - Adult from their own body

Allogenic Stem Cells

- When a stem cell comes from another person (host vs graft), these are known as allogenic stem cells

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Embryonic vs. Adult: The History and Future of the Stem Cell Debate

Caroline P. Torrisi*

Embryonic stem cell research, which requires the destruction of human embryos, has produced widespread ethical concern and debate over the past several decades. This concern has resulted in limiting the potential of scientific and medical advances in stem cell research. However, a scientific development may end the embryonic stem cell debate forever. Recent studies and reports have indicated that adult stem cells, found in various parts of the human body after birth, are more scientifically and medically useful than previously thought. If researched further, adult stem cells may become equal to, or possibly more useful than, embryonic stem cells. This note examines the future of stem cell research and the potential for adult stem cell use to replace that of embryonic stem cells by exploring recent developments in the study of adult stem cells. Section I will examine the biological nature of the stem cell and differentiate between the types and sources of these cells. It will also examine recent advances in adult stem cell research that indicate their immense medical potential. Section II will outline the history of the stem cell debate in the United States, detailing the federal government's refusal to provide federal funding for embryonic stem cell research. Finally, Section III will discuss the need for government action and a

cornea, cord blood, cartilage, fat, and skin are capable of differentiation into cells other than those of their origin.[38] For example, stem cells from a human's bone marrow are capable of giving rise to neural cells and kidney cells, rather than merely acting to repair and replace bone marrow cells alone.[39] While the full potential of adult stem cell application is not yet known, research has shown that, among other possibilities, stem cells taken from various organs and tissues of the "adult" body can reduce brain damage resulting from strokes, treat leukemia and other types of cancer, cure diabetes, restore eyesight and hearing, repair the heart from heart attack damage and blocked arteries, treat kidney failure, delay symptoms of Lou Gehrig's Disease, regenerate nerve cells in multiple sclerosis patients, regenerate muscle in muscular dystrophy patients, and potentially restore paralysis.[40]

One scholar has argued that "adult stem cells have outstanding advantages in terms of immediate clinical application, safety and feasibility over all other sources of stem cells."[41] One major advantage is that adult stem cells pose no risk of immune rejection, which is a common problem in embryonic stem cell treatment.[42] When tissue derived from embryonic stem cells is transplanted into the body, it "runs the same risks

rejection.[44] Another major advantage of adult stem cells is that they are less likely to pose a risk of cancerous development than embryonic stem cells.[45] Embryonic stem cells often "undergo uncontrolled transformation and growth" once transferred into a patient, which can ultimately lead to the growth of tumors.[46]

various studies of adult stem cell differentiation).

[39] *Id.* at 270-72.

[40] John D. Murnane, Esq., *Engineering Eden: Investigating the Legal and Ethical Dilemmas of Modern Biotechnology*, 20 ST. JOHN'S J. LEGAL COMMENT. 71, 80-82 (2005) (detailing advances in adult

Kipp A. Van Camp, DO

- Medical School (DO), University of Medicine and Biosciences, Kansas City, Missouri. USA, 1990
- Family Medicine Residency (DAAFP), University of Missouri, Kansas City, Missouri. USA, 1990-1993
- Former Family Physician (FAAFP), Private Practice, Weston, Missouri. USA, (1993-1997)
- Diagnostic Radiology Residency (DAOCR), Oklahoma State, University, Tulsa, Oklahoma. USA, (1997-2000)
- Interventional Radiology Fellowship (CAQ-IR), Georgetown University, Washington, DC. USA, (2000-2001)
- Radiology and Interventional Radiology Practice, Topeka, Kansas. USA (2001 – present)
- Research: Topeka, Kansas. USA (2011)

My Story: 2000-2011 Minding my own business…

IRB Approved, Medical Research for the Treatment of Various Diseases Using Stromal Vascular Fraction Cellular Therapy, Platelet-Rich Plasma Therapy; with a Review of the Current and Ongoing Results

ALZHEIMER'S DISEASE

Stromal Vascular Fraction Research

Kipp A. Van Camp, DO, DAOCR, CAQ-IR

History:
- Midwest Radiology Institute
- Precise Clinical Research Solutions/Midwest Medical Research Institute

- My Father, Robert Victor Van Camp, 77 y.o. retired DVM, diagnosed with Alzheimer's Disease (AD), 2011
- Family sought any/all available treatments for AD. Contacted Maritza Novas, MD
- Brought Dad to Miami, Florida for first treatment August, 2012. Had mini-liposuction, Followed initial Adistem protocol with collagenase, then SVF infused through peripheral IV
- Second treatment in Miami, Florida, May 2012. At this time, I trained to perform procedure in Kansas

AD Research

- July 2012, talked to Kansas Board of Healing Arts, Topeka, Kansas. USA
- Advised only way to perform this procedure was through IRB approved research
- Wrote AD research protocol
  - **Intravenously Administered Autologous, Adipose-Derived Stromal Vascular Fraction in the Treatment of Alzheimer's**
- Protocol Approved: Sept 26, 2013
  - **Protocol Number**: A3-AZ-3701
- **IRB: International Cell Surgical Society**

IRB Approval Number: ICSS-2013-90 , Approval renewed: September 12, 2014, Valid until September 12, 2015

IRB Approval does not constitute exemption from applicable state, local or federal regulations or requirements, is not a substitute for any required pre-market approval and is reserved solely for investigational studies that fall outside the scope of regulation of the Food and Drug Administration

CERTIFICATE OF APPROVAL

This is to certify that

Kipp Van Camp, DO

Has, on the 26th day of September 2013

Been granted approval by the

Institutional Review Board

of the

International Cell Surgical Society

For the Intravenously Administered Autologous, Adipose-Derived Stromal Vascular Fraction in the Treatment of Alzheimer's Disease

Chair

Secretary

AD SVF Research

- Recruited: 4 AD patients
- Minimal to moderate Cognitive Impairment
- Began treatment: November, 2013

Required Studies prior to beginning treatment:

- SLUMS
  - St. Louis Mental Status Exam
  - Scale is 1 to 30, 30 =Normal
  - Must have Slums above 17 = minimal to early moderate cognitive impairment
- Neurologist Confirming Diagnosis of AD
- MRI Brain
  - No other underlying neurological findings (past CVA, Brain neoplasm, hydrocephaly)
- CT Brain
  - No active hemorrhage or prior hemorrhage with associated encephalomalacia
- SPECT Imaging of Brain
  - Findings consistent with AD
- Diagnostic LP
  - Beta-Amyloid, Total Tau Protein markers

- Treatment Initiated

Couple of items unique to our study

- Miniliposuction completed with sonographic guidance
- Bone Marrow performed with fluoroscopic guidance
- Diagnostic LP performed with fluoroscopic guidance

Couple of Items Unique to our Study and our current Process: Miniliposuction completed with sonographic guidance
Bone Marrow performed with fluoroscopic guidance

Fluoroscopic Guidance

Ultrasound Guidance

Protocol: Order of Treatment and Diagnostic Studies

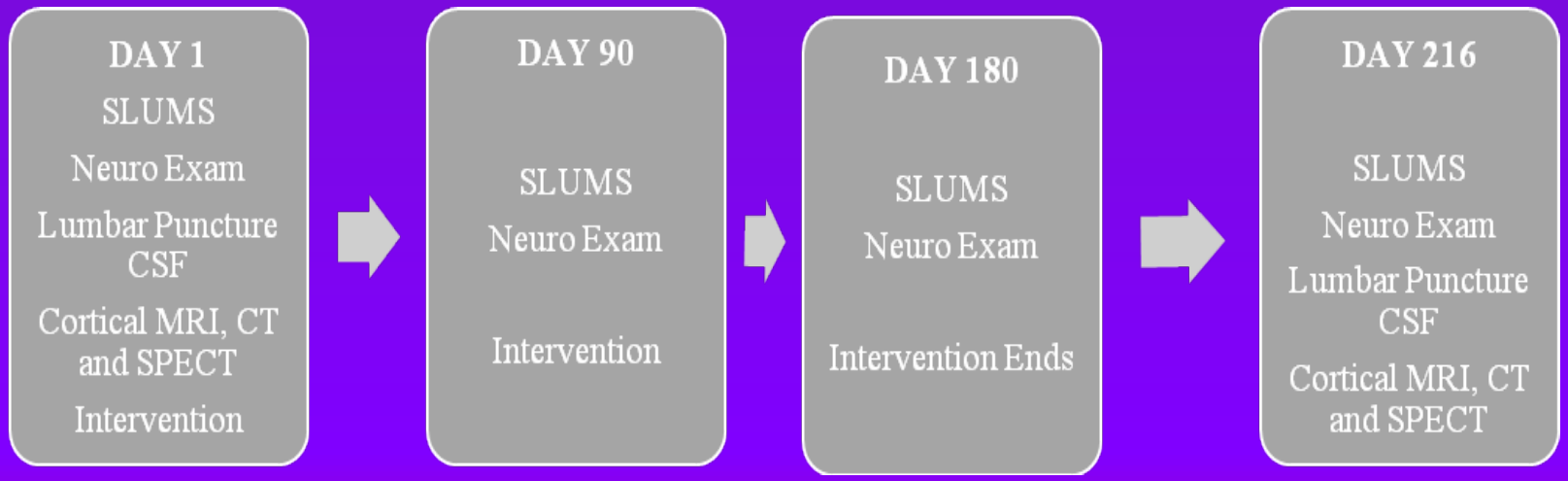
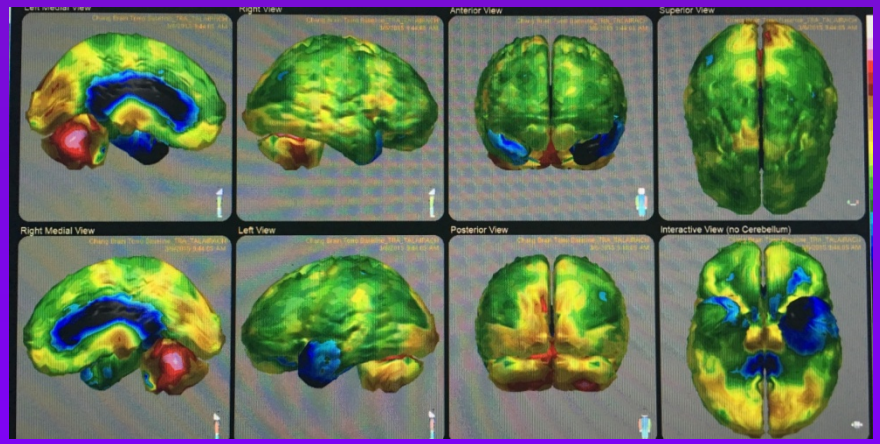


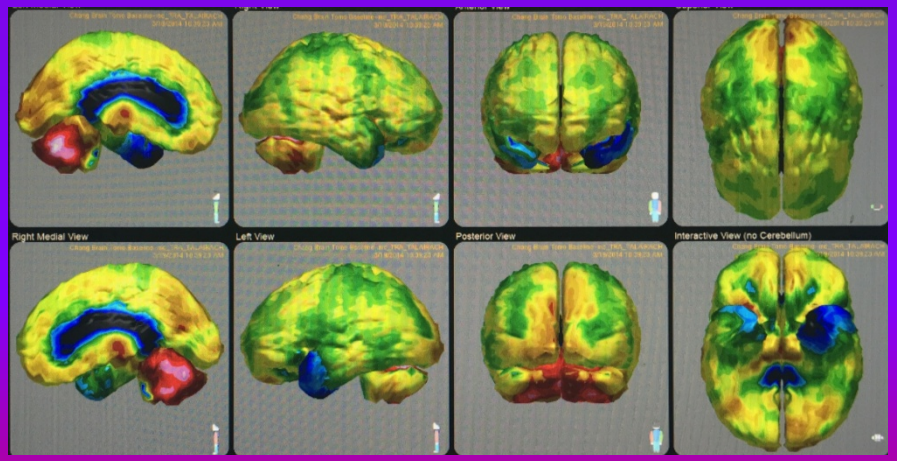
Table 1. Individual Effects of the MSC Intervention within Alzheimer's Patients

Patient	Age	Sex	Onset (yrs)	SLUMS		Beta Amyloid		Tau		Level of Impairment
				PRE	POST	PRE pg/ml	POST pg/ml	PRE ng/l	POST ng/l	
01-000	79	M	18 mo.	18	15	1428	1369	977	911	Minimal
01-001	64	F	2	17	15	1102	1796	41	243	Minimal-Moderate
01-002	79	M	2.5	20	26	1150	806	715	529	Minimal
01-003	71	M	2	20	27	1057	118	566	103	Minimal

Midwest Radiology Institute SPECT Brain Scan

AD Before treatment

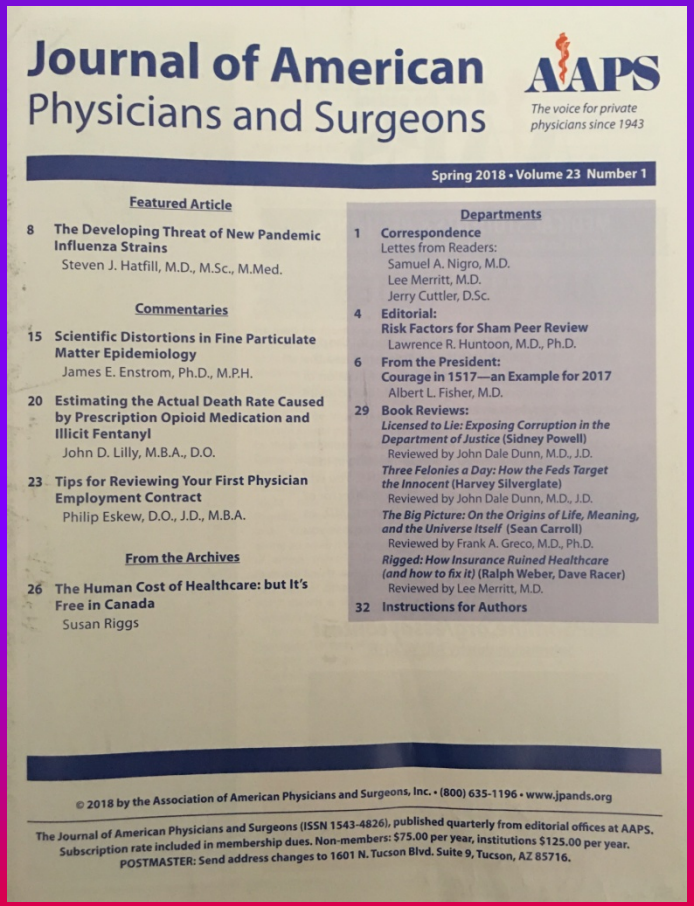




Case Study: Intravenously Administered Autologous Bone Marrow and Adipose-Derived Stromal cells in the Treatment of Alzheimer's disease

- Wrote paper from March 2015-Sept. 2015
- Submitted paper to Journal Translational Medicine, September 2015
- JTransMed asked for corrections: Sept 30, 2015
- Corrections submitted to JTranslMed, Oct. 8th, 2015
- Denied-too small "n"
- December 2015-submitted paper to Journal of American Osteopathic Medical Association
- Denied Publication
- Forgot About Publication for awhile…

Accepted For Publication
Coming in Winter Edition 2019



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Limitations of this study

- Small *n*
- Used both Mesenchymal (miniliposuction) and Hematopoietic (bone marrow) SVF
- Studied B-Amyloid, and Total Tau in CSF
  - Next protocol use: Total Tau and Phosphorylated Tau, and A-B-Amyloid 41
- Included minimally-cognitively impaired and early moderately cognitively impaired AD pts
- **No outside funding**: Patients Paid Cost + 10% to participate in this Phase 1-Investigator Driven Research

Robert Victor Van Camp, DVM
February 9th, 1933
April 7th, 2015

COPD Trial

- IRB Protocol approved, August, 2014.
- 5 patients
- Confirmed diagnosis of emphysema based on Pulmonary Function Studies, Computed Tomography and Chest X-Ray changes, pulmonary s/s
- Screening: Pulm exam, PFT's, PA/Lat CXR, CT Chest
- Treatment x 3 (one treatment every 3 months), Fluoroscopic Guided Bone Marrow Aspirate and SVF, Collection of Platelet Rich Plasma, 1.5 cc's of SVF mixed with 1.5 cc's of PRP nebulized/aeroloslized over 20-30 minute interval, remainder of PRP and SVF given intravenously over 3 hours.
- PFT's repeated 1 week after the second treatment,
- q 3 months repeat of Pulm exam, PFT's, PA/Lat CXR, CT Chest

Midwest Radiology Institute Topeka, Kansas, USA

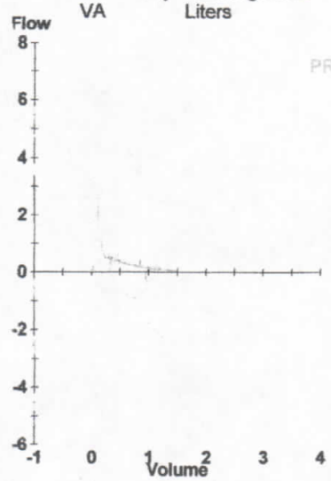
- In-Office: Pulmonary Function Testing

COPD Trial

- Results:
- All 5 patients experienced improved PFT's after 3 treatments
- All 5 patient's had clinical improvement.
- All 5 patient's showed some improved aeration of lungs and decreased inflammation t/o lungs on CT of Chest.

Pt: CG, PFT's: (09/2014)

Spirometry	(BTPS)	PRED	PRE-RX BEST	PRE-RX %PRED	POST-RX BEST	POST-RX %PRED	% Chg
FVC	Liters	2.56	1.49	58	1.41	55	-5
FEV1	Liters	1.96	0.48	25	0.49	25	2
FEV1/FVC	%	77	32		35		
FEF25-75%	L/sec	1.79	0.15	8	0.17	10	15
FEF50%	L/sec		0.16		0.19		15
PEF	L/sec		2.65		2.52		-5
MVV	L/min						
Lung Volumes	(BTPS)						
TLC	Liters	4.73	5.41	114			
RV	Liters	2.12	3.92	185			
RV/TLC	%	44	72				
FRC PL	Liters	2.69	4.45	165			
VC	Liters	2.56	1.49	58			
Diffusion							
DLCO	mL/mmHg/min	21.4					
DL Adj	mL/mmHg/min	21.4					
DLCO/VA	mL/mHg/min/L	4.78					
DL/VA Adj	mL/mHg/min/L						
VA	Liters						



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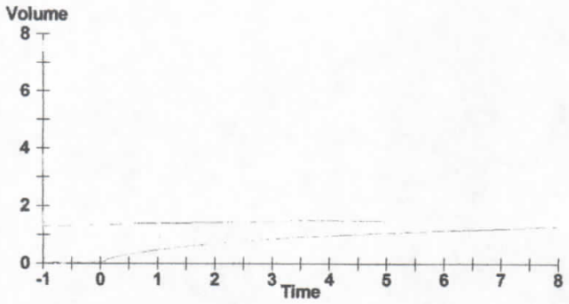
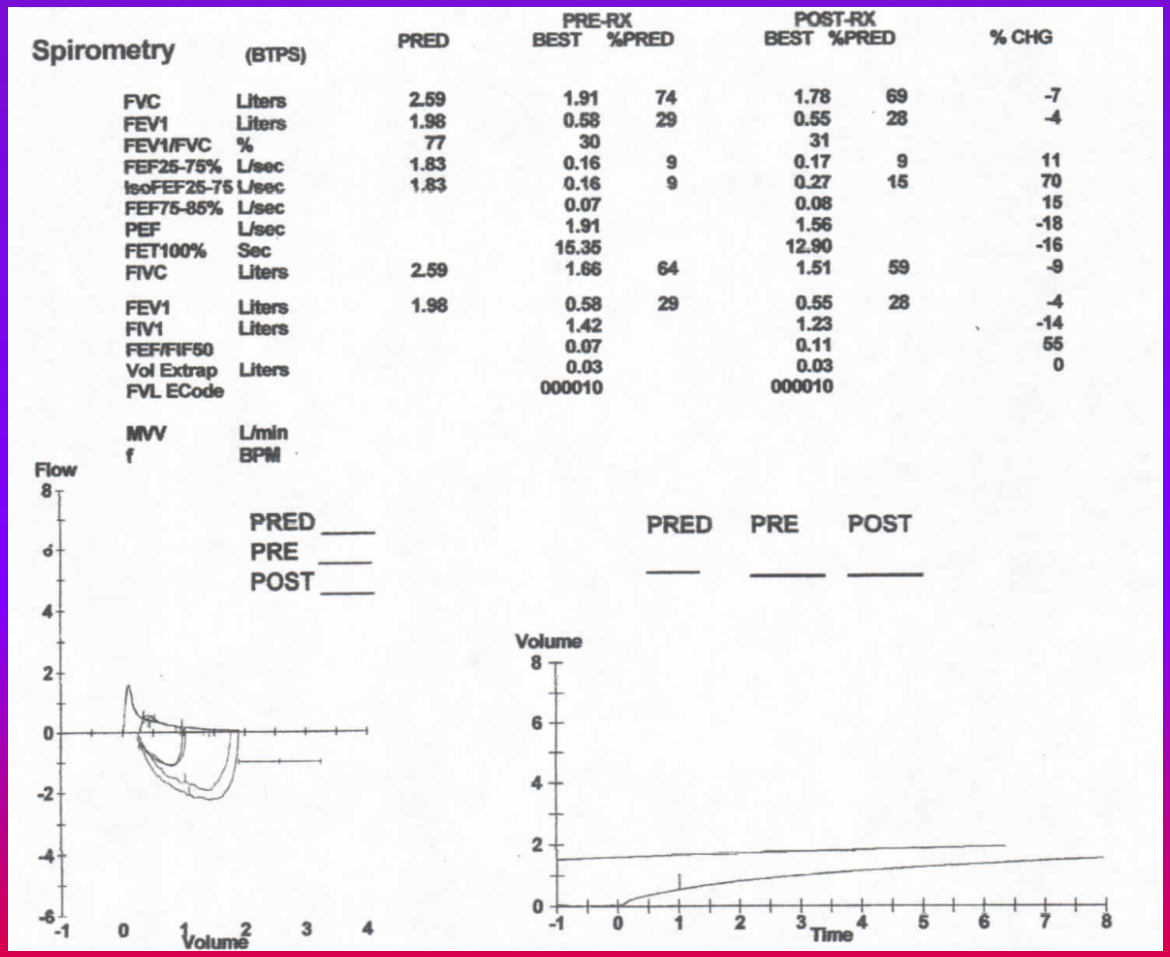


Comments:

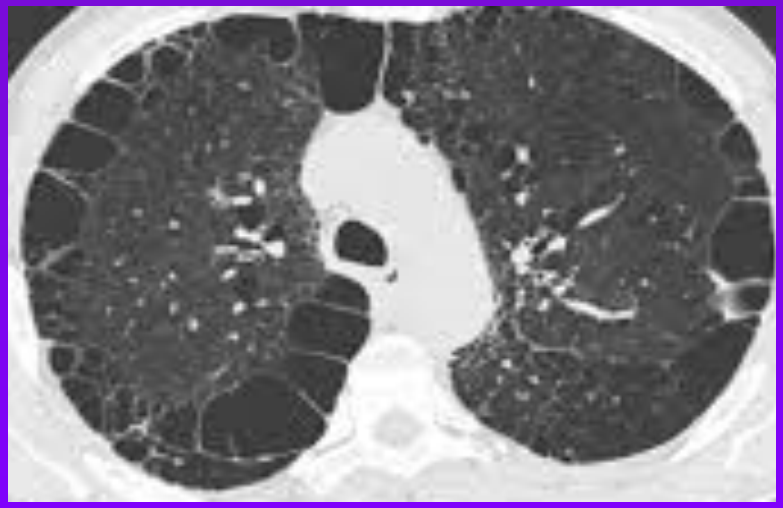
Pt: CG, PFT's (07/2015)

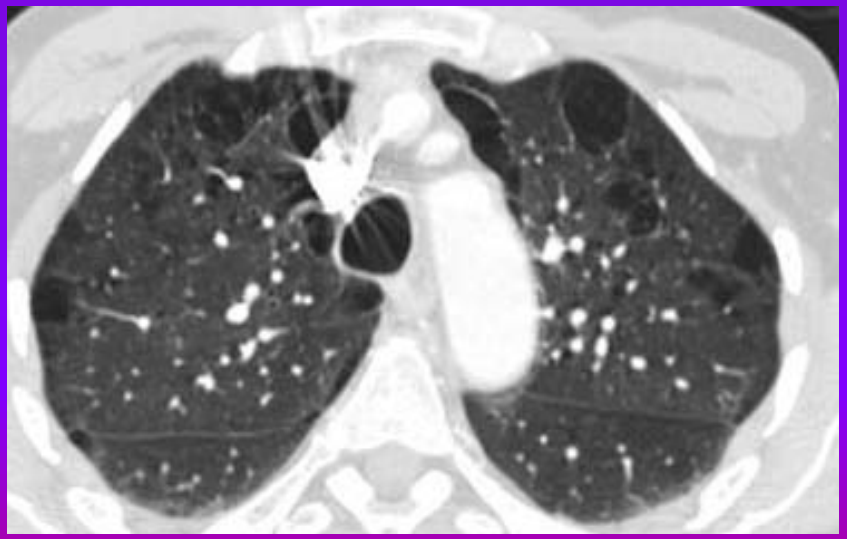


Spirometry (BTPS)

		PRED	PRE-RX BEST	PRE-RX %PRED	POST-RX BEST	POST-RX %PRED	% CHG
FVC	Liters	2.59	1.91	74	1.78	69	-7
FEV1	Liters	1.98	0.58	29	0.55	28	-4
FEV1/FVC	%	77	30		31		
FEF25-75%	L/sec	1.83	0.16	9	0.17	9	11
IsoFEF25-75	L/sec	1.83	0.16	9	0.27	15	70
FEF75-85%	L/sec		0.07		0.08		15
PEF	L/sec		1.91		1.56		-18
FET100%	Sec		15.35		12.90		-16
FIVC	Liters	2.59	1.66	64	1.51	59	-9
FEV1	Liters	1.98	0.58	29	0.55	28	-4
FIV1	Liters		1.42		1.23		-14
FEF/FIF50			0.07		0.11		55
Vol Extrap	Liters		0.03		0.03		0
FVL ECode			000010		000010		
MVV	L/min						
f	BPM						

HR CT Chest





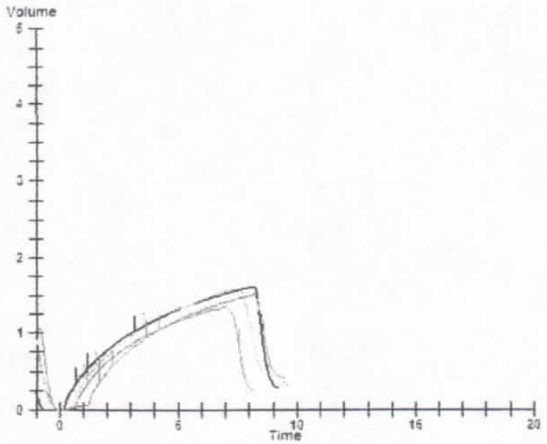
Pt: RC, PFT's (05/2014)

Date: 04/18/14 **Post**

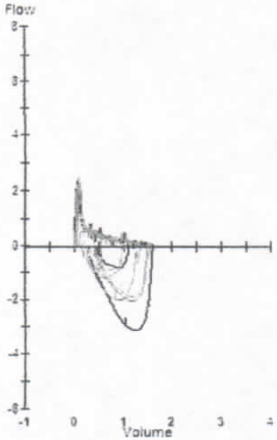
Flow Volume Loop — , - 5400-001

	Ref	Best	% Ref	1	2	3	%Chg
FVC	2.70	1.58	58	1.34	1.58	1.50	-2
FEV1	2.03	0.58	29	0.53	0.58	0.57	6
FEV1/FVC	76	37		39	37	38	
FEF25-75%	1.73	0.25	15	0.24	0.25	0.25	9
PEF	5.24	2.49	48	2.25	2.49	2.28	-9

Trial 3

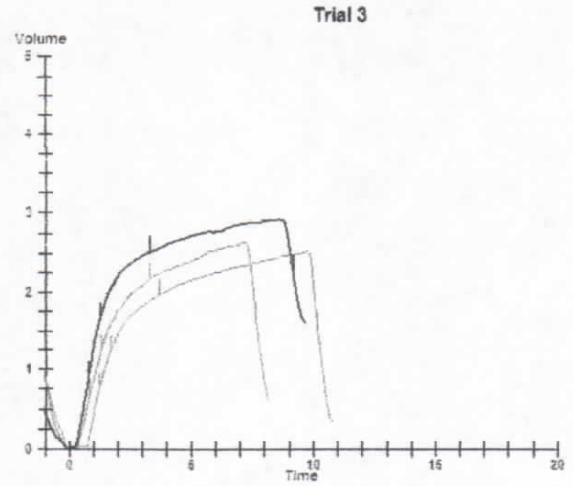


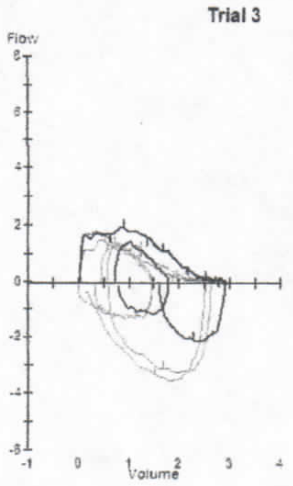
Trial 3



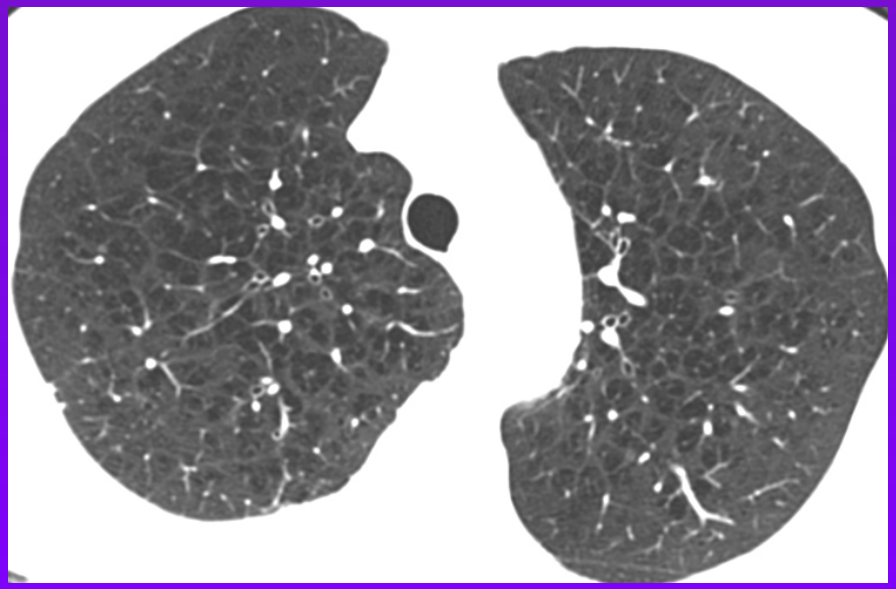
Pt: RC, PFT's (02/2015)

	Ref	Best	% Ref	1	2	3
FVC	3.13	2.92	93	2.52	2.64	2.92
FEV1	2.17	1.71	79	1.27	1.30	1.71
FEV1/FVC	71	59		50	49	59
FEF25-75%	1.42	1.15	81	0.58	0.75	1.15
PEF	5.88	1.96	33	1.80	1.53	1.96

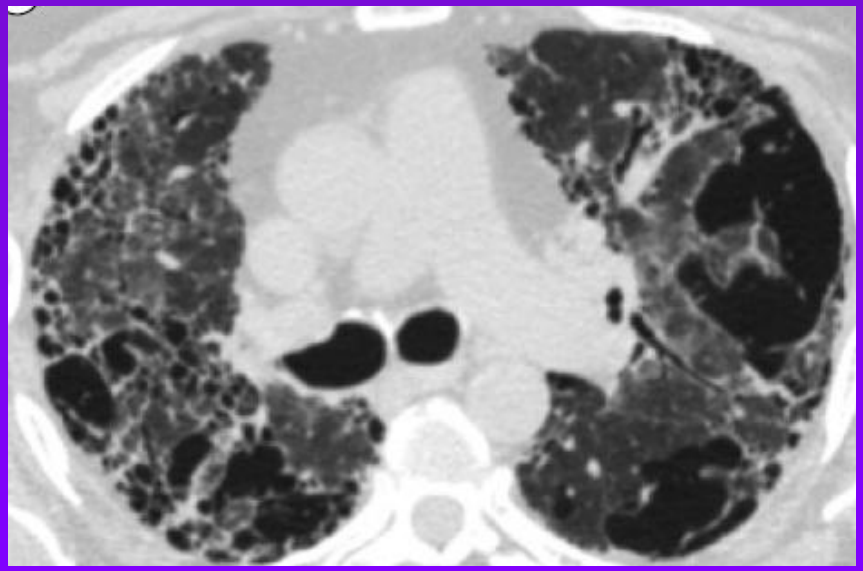


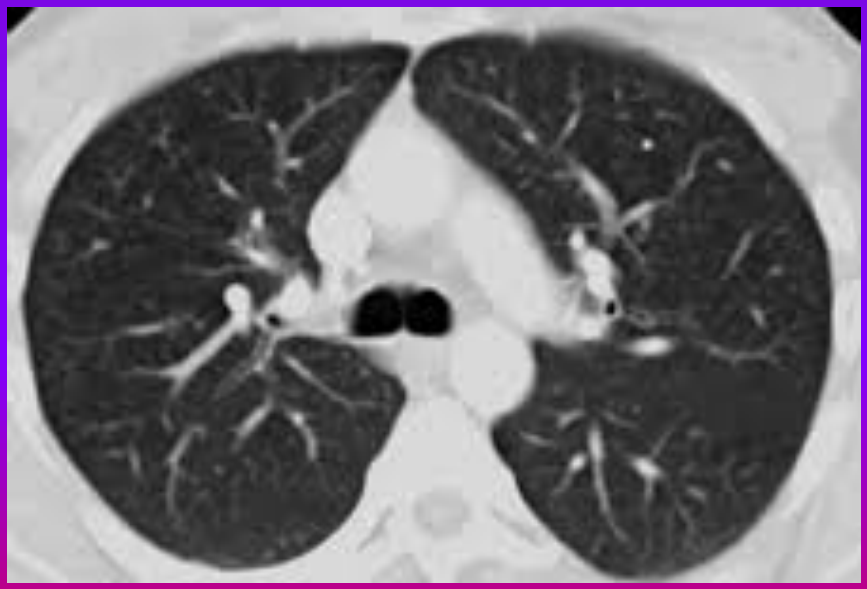


HR CT Chest



HR CT Chest: CG Before Stem Treatment, 3 years later after 9 treatments





Osteoarthritis Trial

- IRB Protocol, August 2014
- 7 patients
- OA of any large joint (shoulder, knees or hips), OA confirmed with radiographic changes (sclerosis, osteophytes, irregular articular surface, narrowed joint space)
- Pre-screening: Plain film x-rays of involved joints (bilateral), MRI of affected joint/s, lab tests (Erythrocte sedimentation rate, Rheumatoid panel to exclude RA, uric acid to exclude gout, CBC, Chemistry panel-23), no recent change in medication, no recent orthopedic surgery, no total or partial arthroplasty of bilateral affected joints.
- Treatment x 3 (one treatment every 3 months), Fluoroscopic Guided Bone Marrow Aspirate and SVF, Collection of Platelet Rich Plasma, 1.5 cc's of SVF mixed with 1.5 cc's of PRP injected intrarticularly (with fluoroscopic guidance and/or ultrasound guidance) into the affected joint/joints, remainder of PRP and SVF given intravenously over 3 hours.

Results:

All 7 patients have experienced clinical improvement (farmer, golfer, retired teacher/needlepoint)

All patients showed improvement in their sed. rates

All patients showed decreased inflammation of the treated joint via MRI imaging

MRI Knee: Before

MRI Knee: After

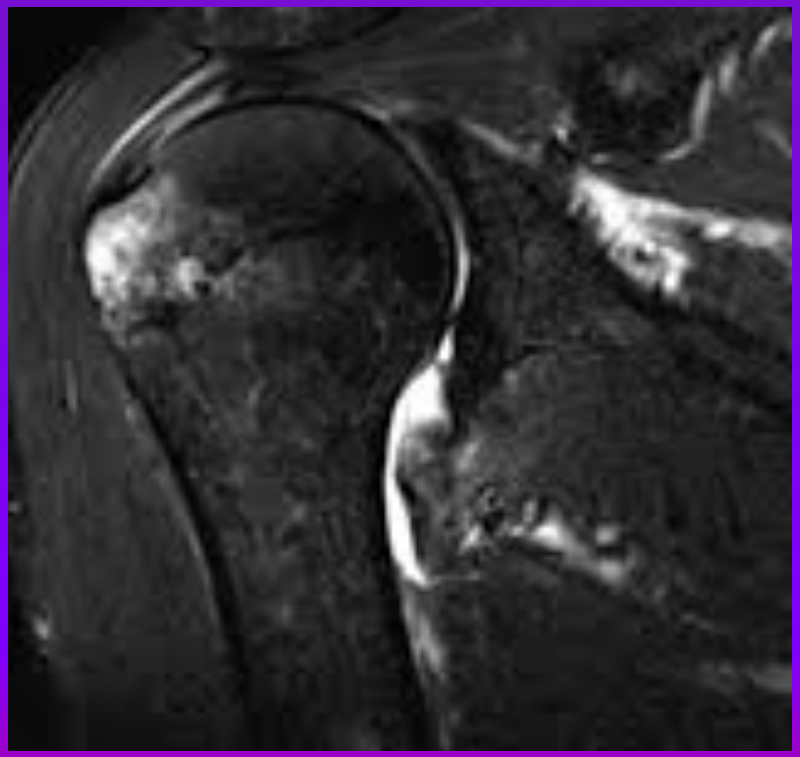
MRI Knee: Before

Before First Treatment

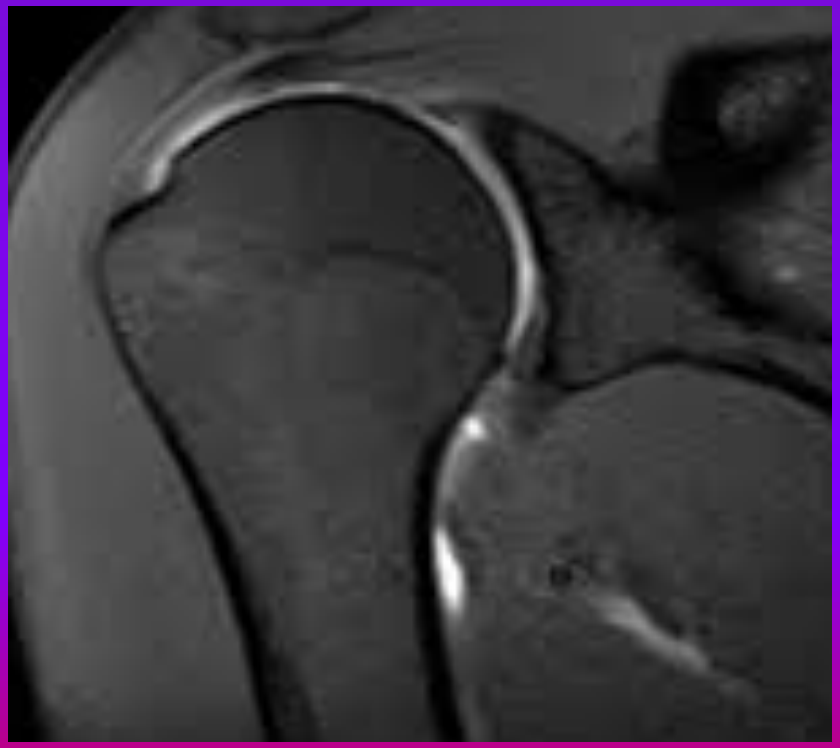
After First Treatment

MRI Knee: After Third Treatment

MRI Shoulder

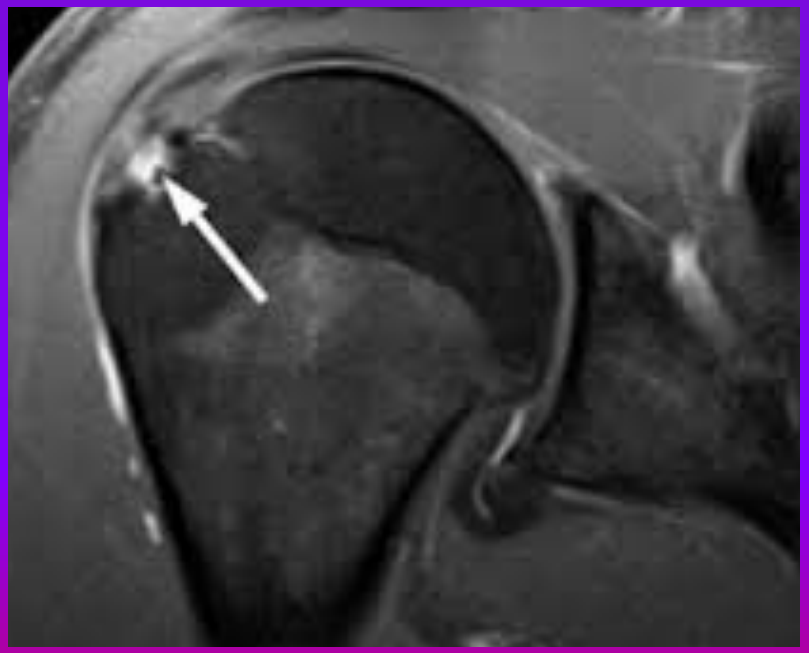


Before First Treatment



After Third Treatment

MRI Shoulder



Before First Treatment

After Third Treatment

Planning:

- IRB approved autism study
- IRB approved Chronic Renal Failure and/or Acute Renal Failure/Glomerulonephritis study
- TBI/CTE study
- Plan to write up the COPD and OA trial results
- Looking for Funding to expand studies

FDA issues:

- Opinion paper suggesting miniliposuction and enzyme dissolution of adipose is manipulation of tissue and not recommended
- Freeze stem cells
- Loosen reigns for funding
  - Currently, in USA, pets/animals have greater chance for uncontested adult harvested stem cell therapy than human patients

Future Possibilities:

- One time harvesting of bone marrow and/or adipose.
- Collect approximately 1 years supply of SVF; Use only the amount needed for that specific treatment and freeze the rest.
- At each appropriate interval, request the necessary portion of the cellular sample; Mix with freshly collected PRP at each treatment interval.
- Collect specimen (BM/Adipose) and send to cryo lab; Grow/clone cells in the lab; Patient only has one initial harvesting.

OPINION

- We need many more US studies with much higher *n* to get America on board with this technique

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Kipp, Tracy, Kolby, and Weston

December 1995

December 2016

1929 Dodge Victory 6 Sedan

The Van Camp Family

Hobby Farmers!