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Whangarei

Friday, August 12, 2016

FULLY BOOKED

16:30 - 18:30 WS #53: Rheumatology Forum: Gout; Biologics; Stem Cells; Early Intervention in RA (120mins not repeated)

(Room 2)

Rheumatology Forum

The Emerging Role of Stem Cells in Arthritis



Peter Chapman-Smith
GPCME Christchurch August 2016

Stem Cell Therapy

- What is “Regenerative Medicine”
- Utilise own tissue for healing/repair
- Unique repair of damaged tissue
- Experimental
- Self funded

Innovative New Medical Rx

- Arthritis - OA, joint damage
- Autoimmune Disease
- Neuro: MS, Parkinsons, ALS, stroke
- Urology - interstitial cystitis, ED, Peyronies.
- Ophthalmology - Sjogrens, SMD, Glaucoma
- Dermatology - lichen planus, psoriasis

Osteoarthritis

Pre 2010: Panadol, quads regime, bike, physio, NSAIDs, HA..... TKJR

Post 2010: Autologous adipose derived stem cell Rx - IV and IA

- Less cost, avoid painful rehab months, no guarantee surgery any better
- Usual 1x treatment 3-4 hours
- Anti-inflammatory, Repair, Improve function
- Reverse cycle inactivity, obesity, depression
- **Worst outcome** - ineffective, can repeat SCs or choose surgery
- **Best outcome** - improved QOL, normal function, no need for surgery
- Longevity - unknown

Orthopaedics is changing - defer or replace joint replacement

Dr Peter Chapman-Smith
Director of NZ Stem Cell Centre Team

Sports Physician 23yrs

Anaesthesia 10yrs

Liposuction 9yrs

Family Medicine 24yrs

Interest in stem cell therapy 6yrs

Affiliated to Cell Surgical Network (USA)

Member of International Society of Cellular Therapy.

Stem cell recipient.

Damage



Repair



Regeneration



Do Patients Like it - Testimonial 1

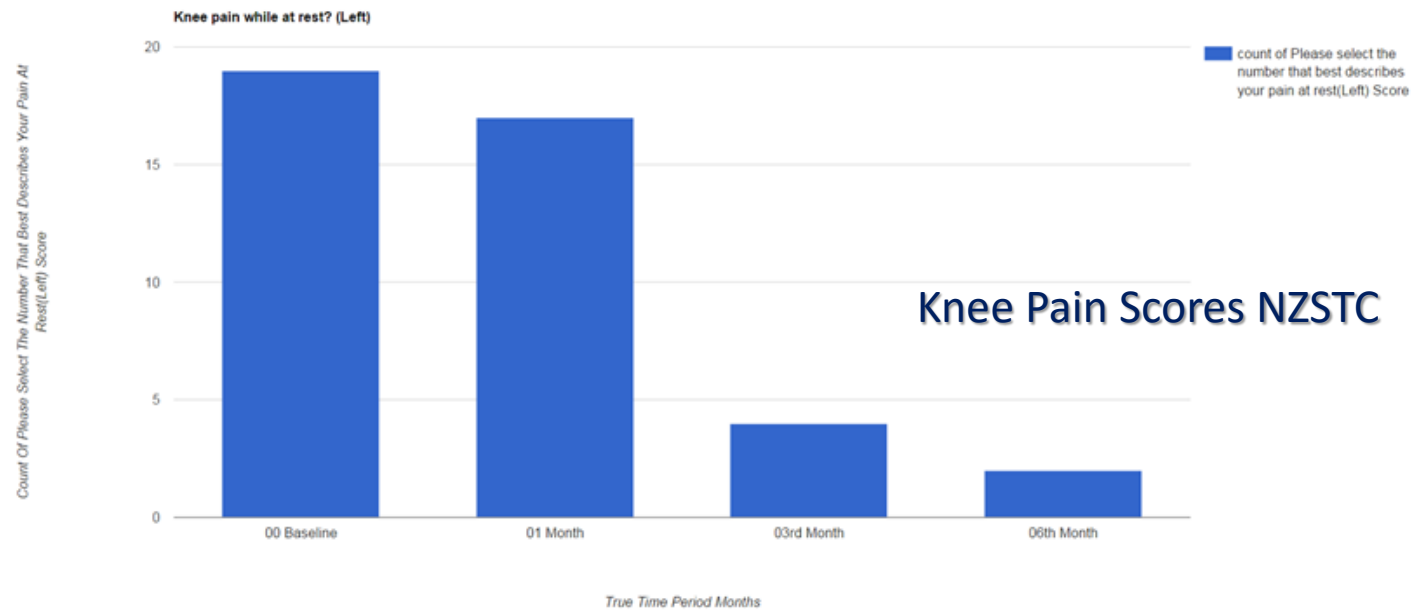
61yr old woman - deferred free TKJR bilateral.

- ✓ To live pain free, to be able to live with movement, to be able to walk with out pain and to start to exercise again is short of a miracle.
- ✓ From not being able to walk up or downstairs, having slide on my bottom to get into my house , even after building a ramp was put in that I can now walk freely. Without any inflammation or locking of my knees or any swelling or any painkillers. Two years of hell I had been through and hardly able to bare each day, this trial procedure is what I would call a miracle for me.
- ✓ From the day stem cell transfer was completed the swelling stopped. My knees didn't lock any longer. I have not had any falls since which were also a regular occurrence. This week I planted 500 trees on a hillside ,where not so long ago I couldn't even walk up a hill let alone even attempt to try this activity.
- ✓ As for the pain! I have not taken one Diclofenac, Oxycodone, or Tramadol since the transfer. Nor have I had to use crutches or a walking stick since.

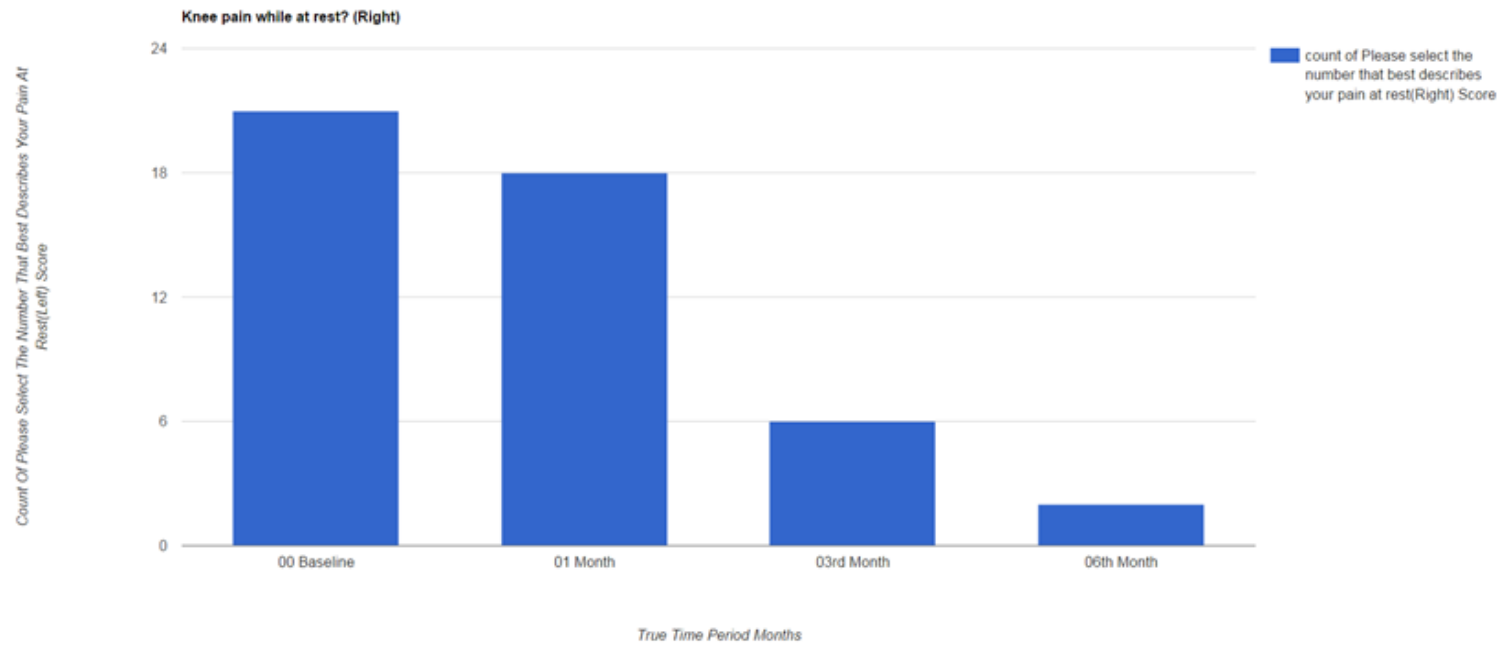
Patient Testimonial 2 - SVF L knee

Prior TKJR R knee, Male 62yrs.
Deferred 2nd TKJR.

- ✓ severe osteoarthritis in my left knee and in constant pain
- ✓ Having suffered with this affliction for a number of years, it was with utter astonishment that I left the clinic that day totally pain free.
- ✓ It was as if a switch had been turned, no more searing pain when driving the car, walking or just sitting at my desk, no more throbbing in the night - the pain had suddenly and inexplicably gone.
- ✓ These treatments are poles apart. The physical, mental and monetary costs of full knee replacement surgery requiring hospitalization, rehabilitation and four months off work, versus local anaesthesia, a little discomfort around the site during stem cell collection and for a few days afterwards, a day off work and no rehabilitation or pain at the end of treatment, make the stem cell option a very attractive alternative indeed.



Knee Pain Scores NZSTC



Cell Surgical Network - LA

- Founded Dr Mark Berman, Dr Elliot Lander
- 1st study adipose-derived SCs - IRB approved research protocols with FDA
- Customized equipment
- “*Cell Surgery*” concept
- 1st International human research network (2010)
- Multinational, multicenter network

SVF SAFETY & EFFICACY STUDY

Online database

Subjective outcome data

Collected D7, D30, 3 mthly 2 years

Patent registry - adverse events

July 2010 onwards

CSN : 1st 1000 patients

Condition Type	No. Patients per Condition	Responsive / Non-responsive	Percentage Responsive
Knee/s	381	310/71	81.00%
Hip/s	53	47/6	89.00%
Shoulder/s	70	59/11	84.00%
Back	58	47/11	81.00%
Elbow/s and/or Wrist/s	14	11/3	79.00%
Foot/Feet and/or Ankle/s	15	11/4	73.00%
Autoimmune	75	56/19	75.00%
Pulmonary	61	35/26	57.00%
Cardiac	19	13/6	68.00%
Neuro-degenerative	153	97/56	63.00%
Erectile Dysfunction	19	12/7	63.00%
Peyronies	15	11/4	73.00%
Interstitial Cystitis	25	21/4	84.00%
Urologic	11	8/3	73.00%
Ophthalmologic	6	5/1	83.00%
Lichen Sclerosis	3	3/0	100.00%
Other	22	18/4	82.00%
Total # of patients researched =	1,000	Total percentage responsive =	76.40%

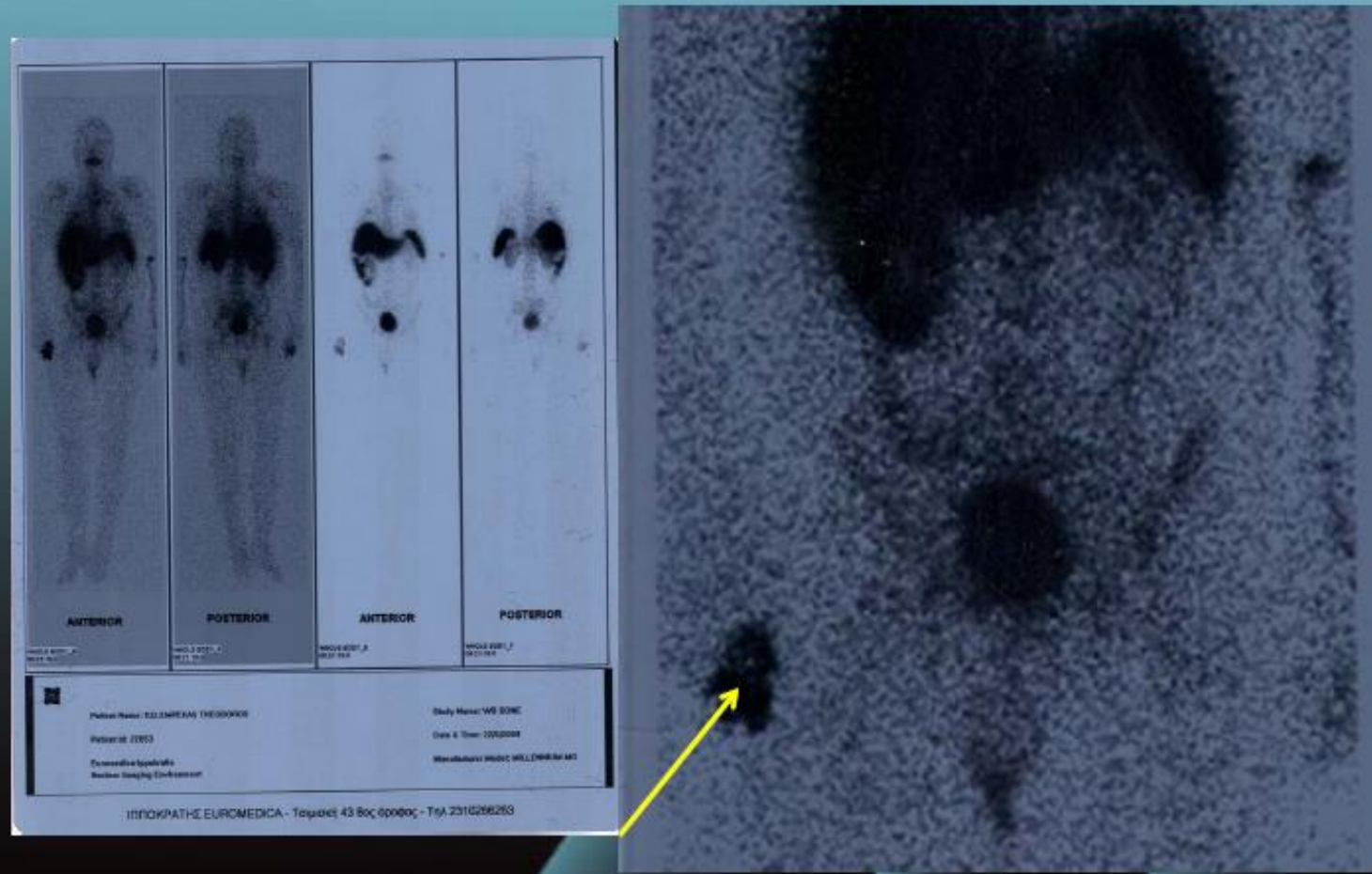
“Regenerative Medicine”

- Utilise stem cells and growth factors
- Repair/replace tissue or lost organ function from damage or congenital defects
 - Create living, functional tissues
- Stimulate previously irreparable organs to heal themselves

Stem Cells - Action

- homing properties to inflammation, tissue damage
- proliferate (replicate)
- differentiate (turn into other specific cells or tissues)
- influence other cells (paracrine effects) – mRNA exchange
- communicate and coordinate cell actions - “the conductor”
- messaging mediated cytokines/GFs

Gamma-camera scan of whole body of cerebellar atrophy
patient after tracing of stromal vascular fraction cells
(^{99}Tc -HMPAO)



Autologous adipose tissue-derived stromal vascular fraction cells application in patients with osteoarthritis

Michalek, J, Moster R, Lukac L, Proefrock K, Petrasovic M, Rybar J, Capkova M, Chaloupka A, Darinskas A, Kristek J, Travník J, Jabandziev P, Cibulka M, Holec M and Jurik M

- 1128 patients
- 1 to 4 intra-articular injections of SVF (total 1856 joint injections)
- Followed up 12 – 50 months later

“No serious side effects, systemic infection or cancer was associated with SVF cell therapy.”

“at least 50% Score improvement was documented in 91% of patients 12 months after SVF cell therapy”

FDA Registered Trials

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

Study # NCT01813279 Safety, tolerability and potential efficacy of injection of autologous adipose-derived stromal vascular fraction in the fingers of patients with systemic sclerosis: an open-label phase I trial.

Study # NCT02276833 Use of Autologous Adipose-Derived Stromal Vascular Fraction to Treat Osteoarthritis of the Knee

Study # NCT02357485 ADSC Injections for Pain Management of Osteoarthritis in the Human Knee Joint

No serious adverse events reported in any of these trials.

2 TYPES OF STEM CELLS

- **Embryonic** (foetal) - cord blood, whartons jelly
- **Adult Mesenchymal** (AMSC) - blood, BM, fat

Embryonic Stem Cells

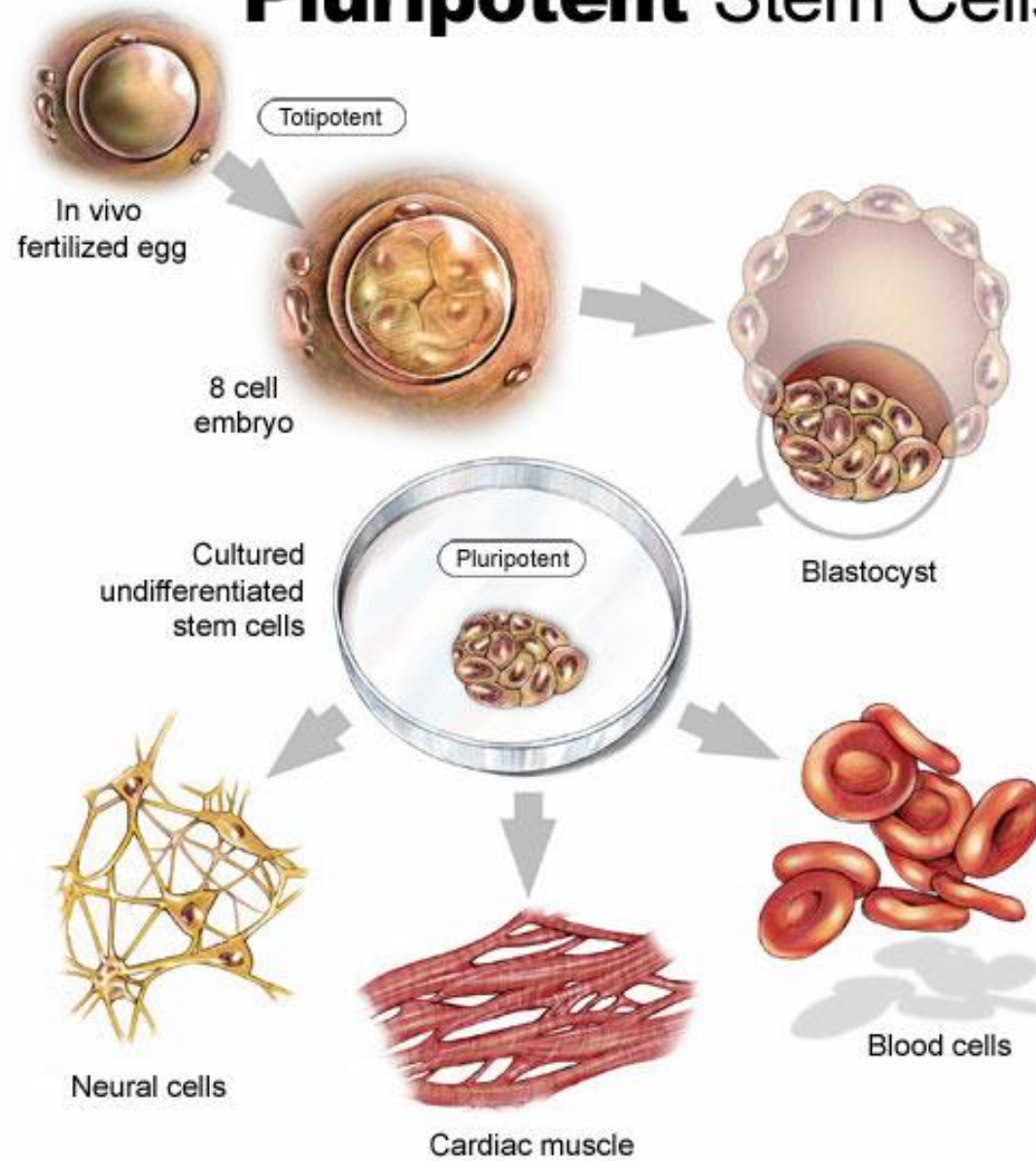
- Can turn into any type of body tissue
- Moral & ethical issues (harvest ... death of “life”)
- Source aborted human embryos, IVF remnants
- Different DNA from host
- Can form teratomas

Adult Mesenchymal Stem Cells

- Bone marrow - continual flow
- Fat - abundant source, **2500 x > BM**
- Multi-potent
- No moral or ethical issues
- Easily repeat harvest
- Cryo storage available



Pluripotent Stem Cells



AMSCs can produce

- ✓ Bone
- ✓ Cartilage
- ✓ Muscle
- ✓ Nerve tissue
- ✓ Blood vessels
- ✓ Connective tissue
- ✓ Fat

Caplan 2011, Tissue Engineering 16; 2415-2417 MSCs

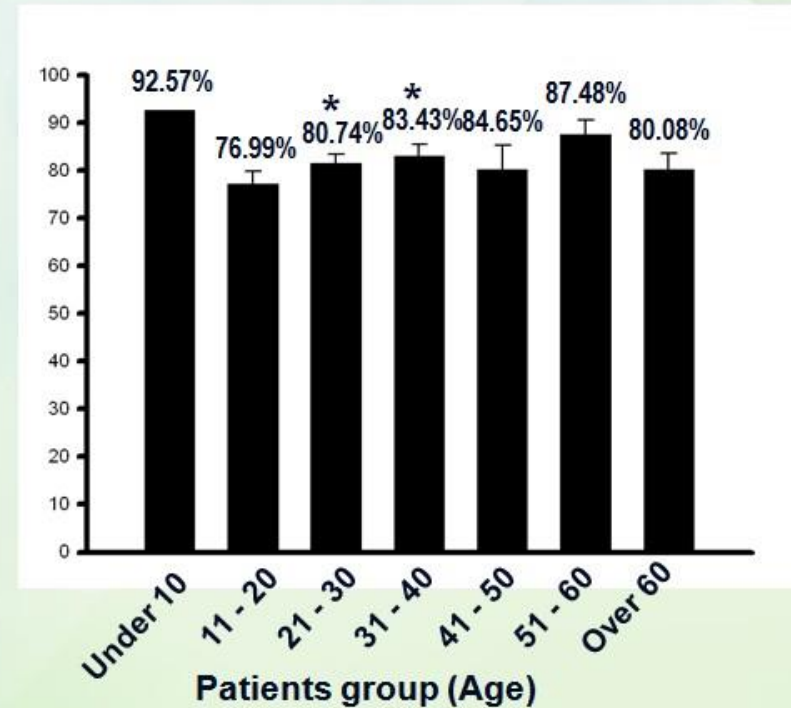
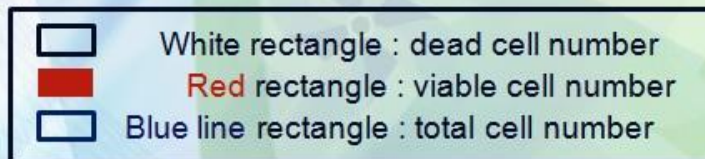
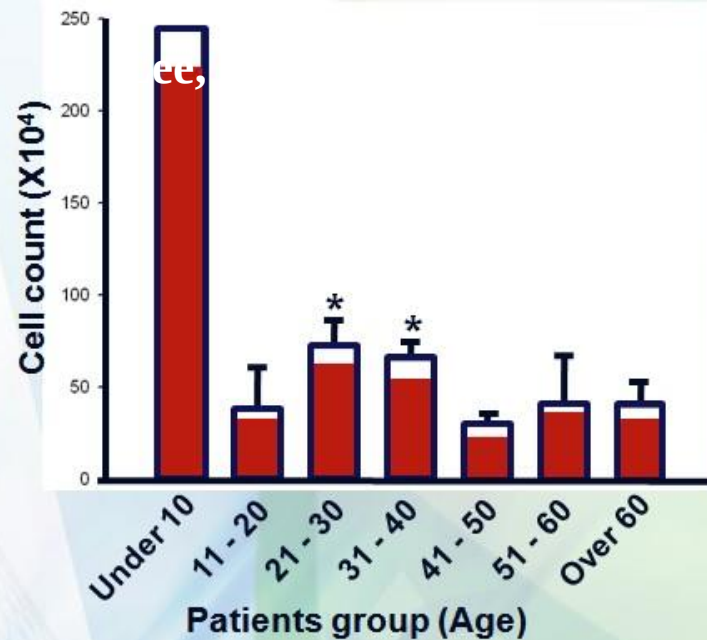
Sources of Adult Mesenchymal Stem Cells

- ALLOGENEIC - other humans
- AUTOLOGOUS - your own body
 - same host DNA, no rejection.
 - lower risk of bacterial/viral infection.

MAIN SOURCES - ADULT STEM CELLS

- Bone marrow : (1:20,000 cells), decline with age
- Fat : 1 gm fat =
1M Adipocytes + Adipose Stem Cells + vascular endothelial cells + other cells
- Low numbers in other tissues (cord, organs)

Cell numbers in 1cc fat tissue



* p < 0.5

Total 72 cases (Under 10 : 1 case, 11 - 20 : 2cases, 21 - 30 : 27cases, 31 - 40 : 19cases, 41 - 50 : 16cases, 51-60 : 4cases, over 60 : 3 cases)

Growth Factors (cytokines)

- Polypeptide signalling molecules
- Affect neighbouring cells
- Initiate cellular repair by stem cells

Why Inject Additional Stem Cells?

- Larger numbers affect therapeutic changes
- Stem cell BIOAVAILABILITY
- Dormant cells made available to damaged tissue
- Exert local and systemic changes

Recent Technological Advances

- New equipment and enzymes
- Adipose derived stem cells easily available
- Safe - local anesthesia, autologous cells
- Abundant numbers of cells
- Procedure takes 3 hours total

SVF - “STROMAL VASCULAR FRACTION”

- Fat is rich in AMSCs + natural growth factors
- T regulatory cells, precursor endothelial cells, preadipocytes, anti-inflammatory M2 macrophages, many cytokines, lymphokines , VegF , Interleukin1
- Over 40 ingredients in a “soup”

Deployed at the NZ Stem Cell Treatment Centre

PRP = Plasma Rich Plasma

These are not stem cells

- PRP : no nuclei, no DNA
- Cellular fragments containing GFs
- Contains WBCs, macrophages, fibroblasts
- Issued into circulation, degranulate and effect repair.
- Aggregate and clot together as plugs
- Incoordinate action
- Joint injections - **temporary effect**, 2-3 mths
- Usual 2-3 injections monthly

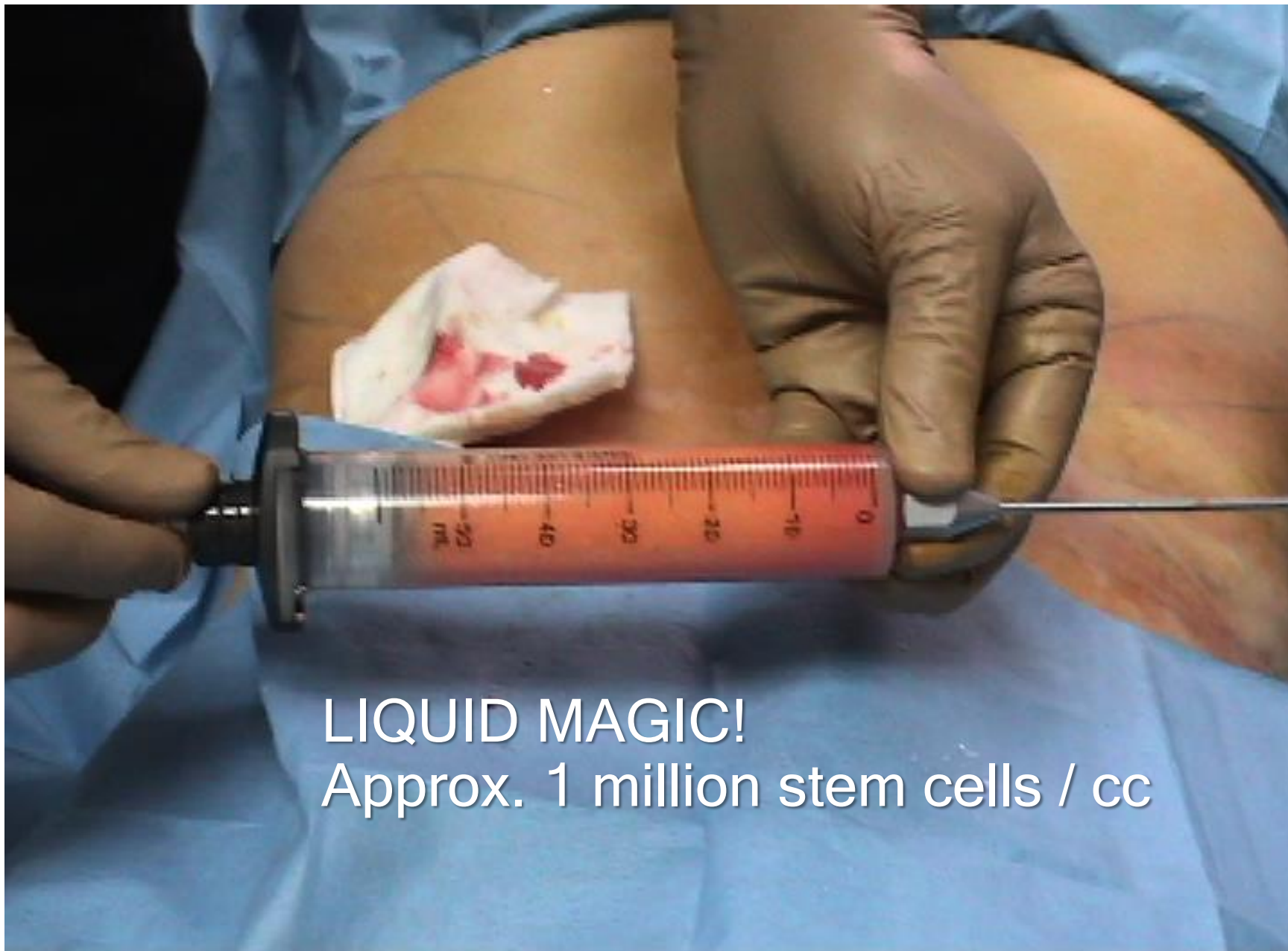
Preparing SVF

- Harvest fat with local anesthesia
- LA toxic to AMSCs
- Centrifuge to concentrate fat
- Enzyme digestion collagen binding fat & stem cells
- Remove stem cells/SVF -“closed” system
- Filtered to 100 microns
- Procurement takes 70-90 minutes





NZ Stem Cell Treatment Centre ; Regenerative
Medicine NZ.



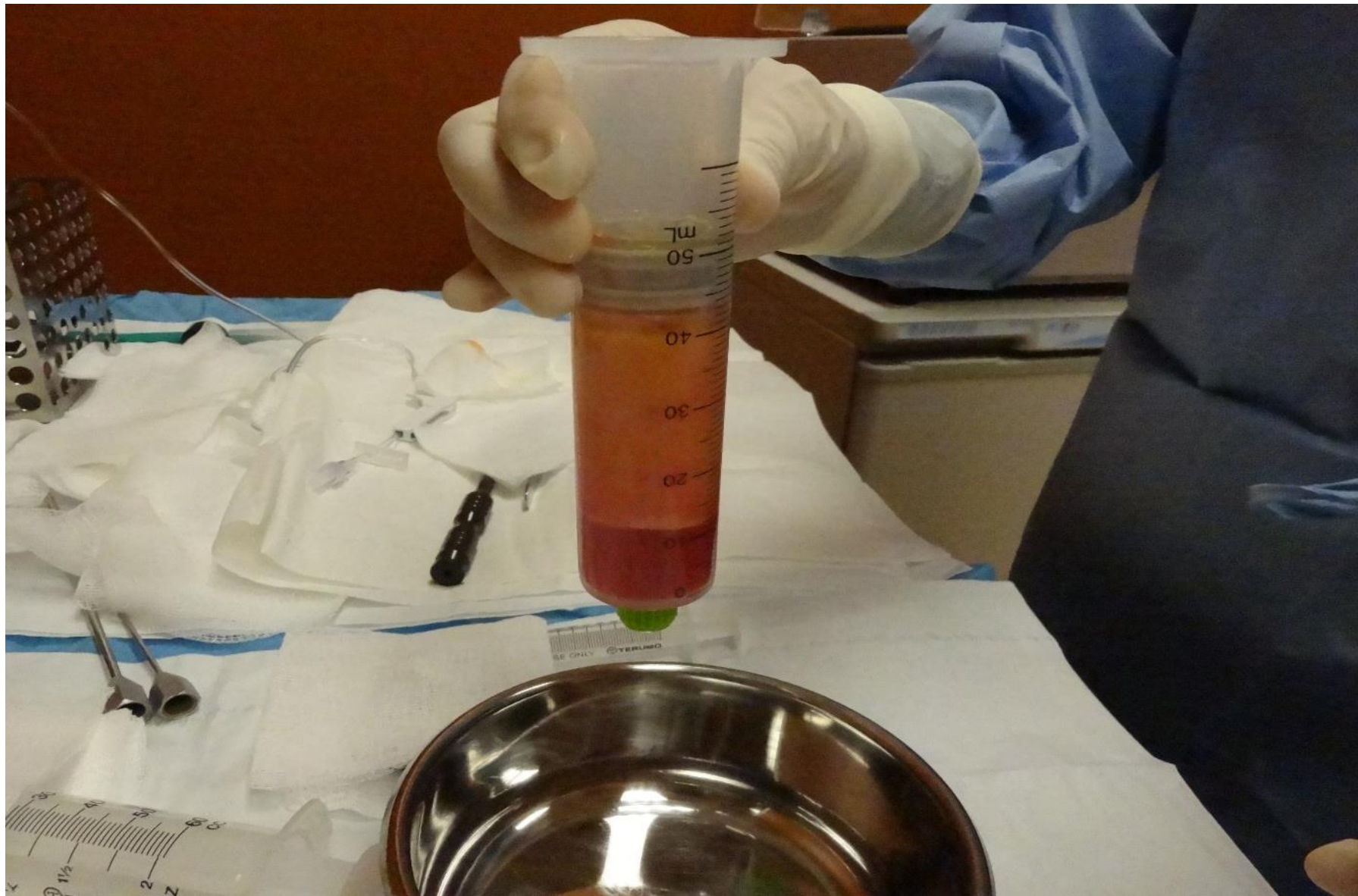
LIQUID MAGIC!
Approx. 1 million stem cells / cc

Surgical Prep - Closed, filtered



Centrifugation





NZ Stem Cell Treatment Centre ; Regenerative
Medicine NZ.

Add Collagenase



Shake gently



Incubate.



Remove fat , add wash solution



Processing , filtering



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Medicine NZ.

Filtered adaptor

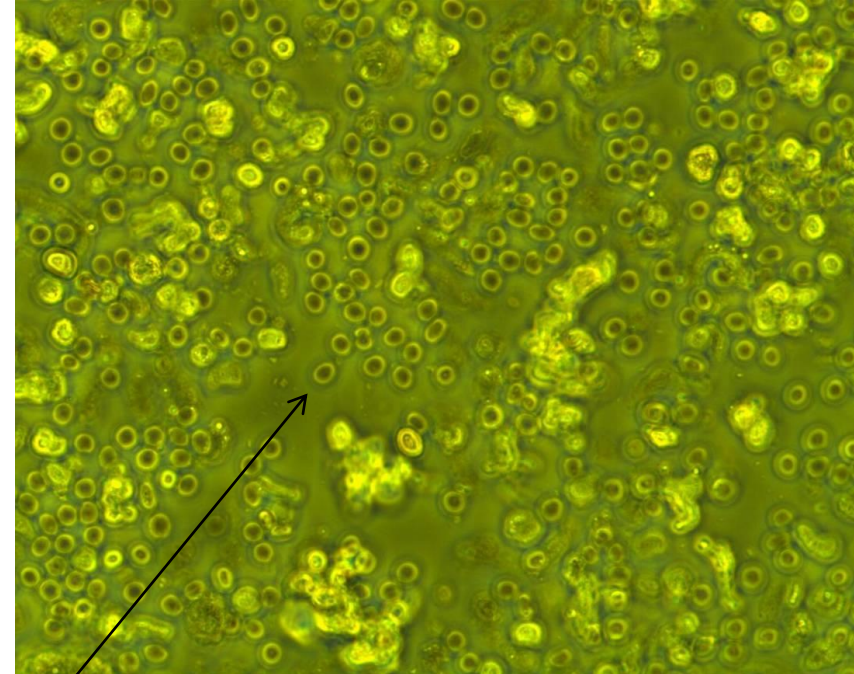
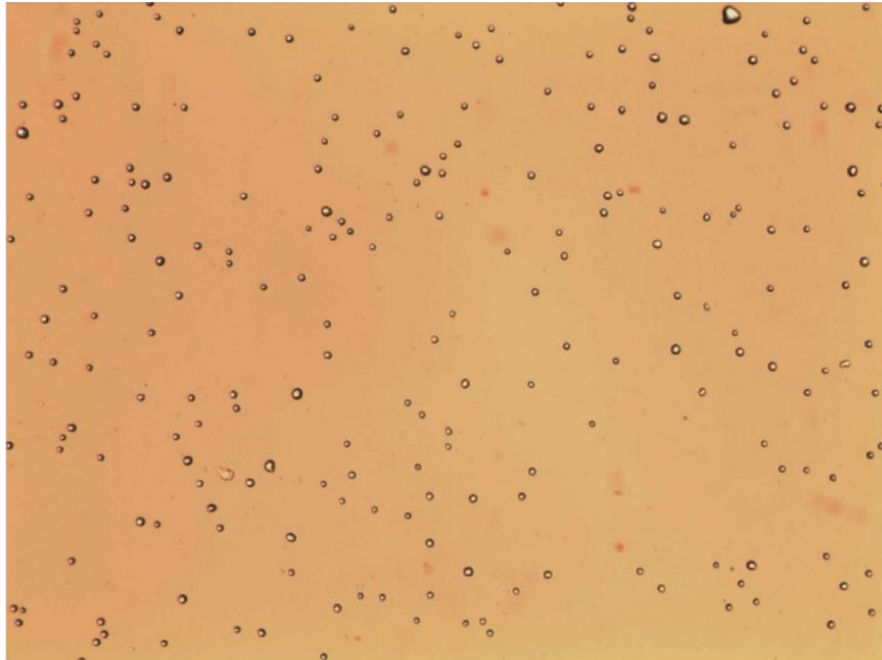




NZ Stem Cell Treatment Centre ; Regenerative
Medicine NZ.

Cell Counter – Invitrogen

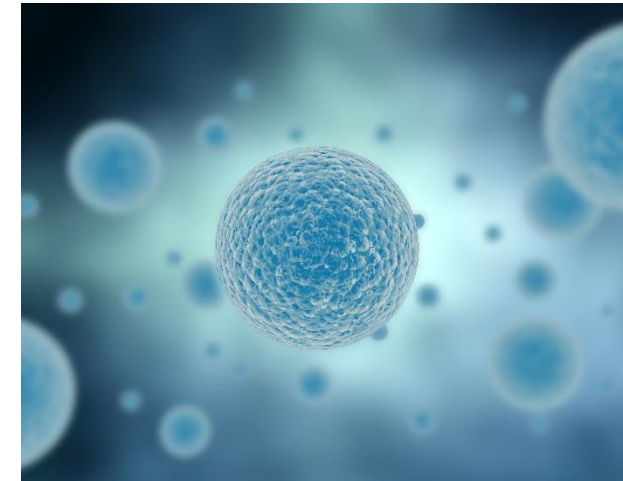
> 10 micron size, numbers, viability recorded



Stem/progenitor cells

200 X magnification

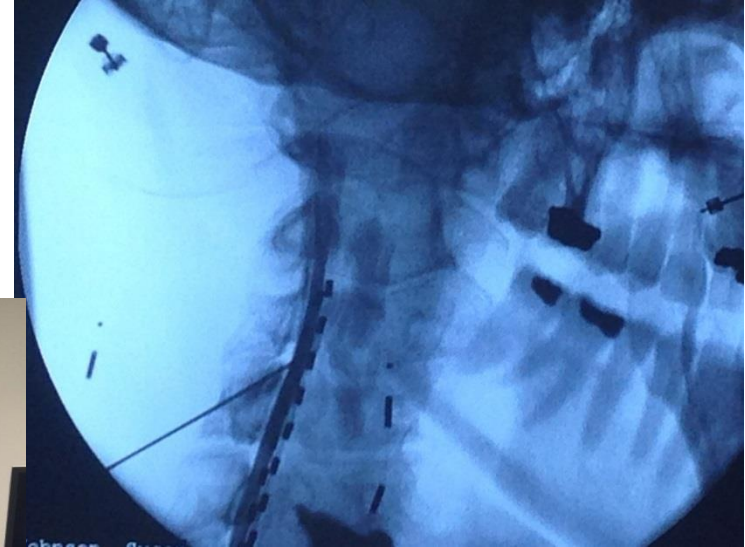
SVF Deployment



- Inject affected joints, damaged soft tissues
- Fluoroscopy or US
- IV injection for systemic changes
- Spinal, extradural, caudal, foraminal injection
- In & around tendons
- Intra-arterial : body, brain, extremities
- Sterile technique, LA to skin only
- Transportable to remote locations

Pain Clinic - Manhattan, Kansas

Cervical Epidural under Fluoroscopy



NZ Stem Cell Treatment Centre ; Regenerative
Medicine NZ.

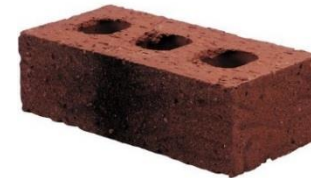
What is Unique about SVF?

- ✓ REGENERATIVE
- ✓ ANTI-INFLAMMATORY
- ✓ IMMUNO-MODULATORY

Onset of Response - SVF

1. Immediate - anti inflammatory
2. Delayed - regenerative, over months

Wait for the “**Stem Cell Moment**” (incredulity)



“Expanded” Cells

- Lab grown to increase SC numbers
- ? Less effective
- Risks of infection, patient ID
- Only culturing cells (need “the soup”)
- Drug regulations - FDA
- More is not necessarily better

Orthopaedics, Musculoskeletal, & Sports Medicine

- Spinal discs, facet arthritis
- Chronic LBP, neck pain, SI joints, coccydynia
- Hips, knees, ankles
- Tendons, ligaments
- Shoulders, elbows, wrist, hands, IP joints.
- Shoulders - can take 2-3 months to improve
- Sports Injuries

SVF far superior to PRP and ABIs.

Prior to SVF deployment

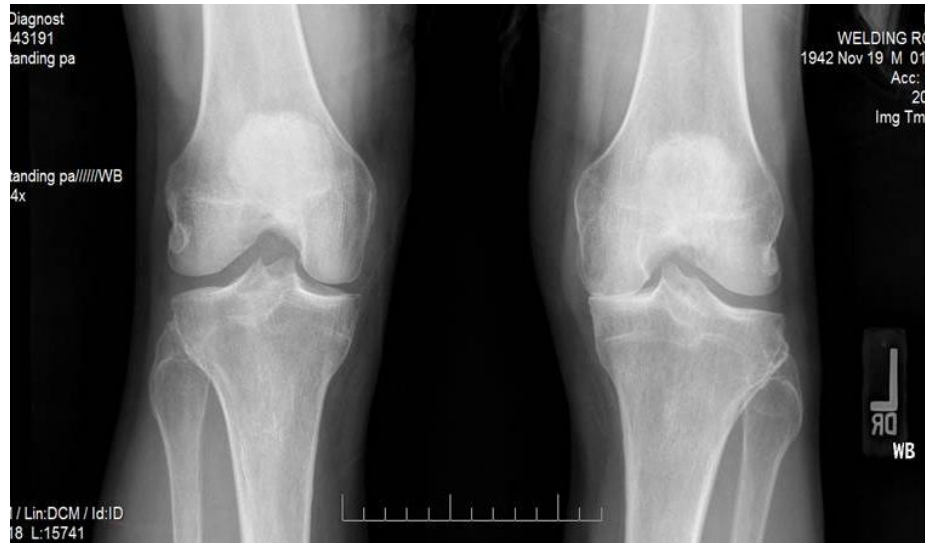


4 months after SVF deployment



Before and After Comparison

Prior to SVF deployment

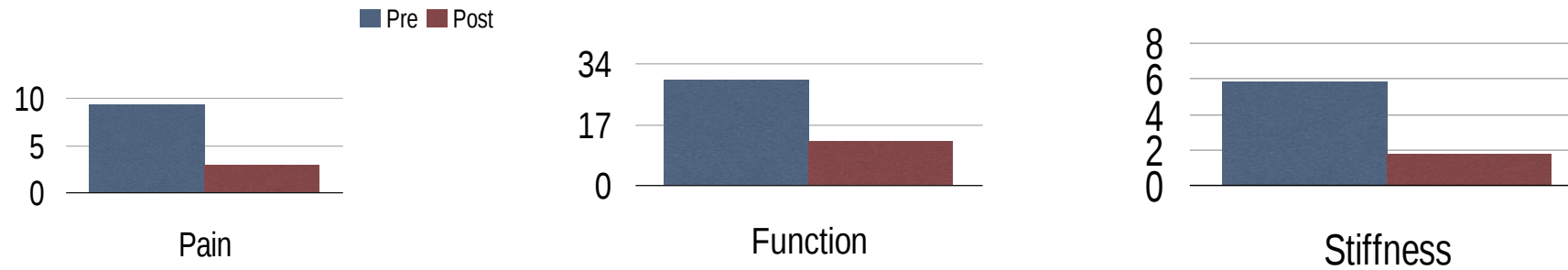


4 months after SVF deployment



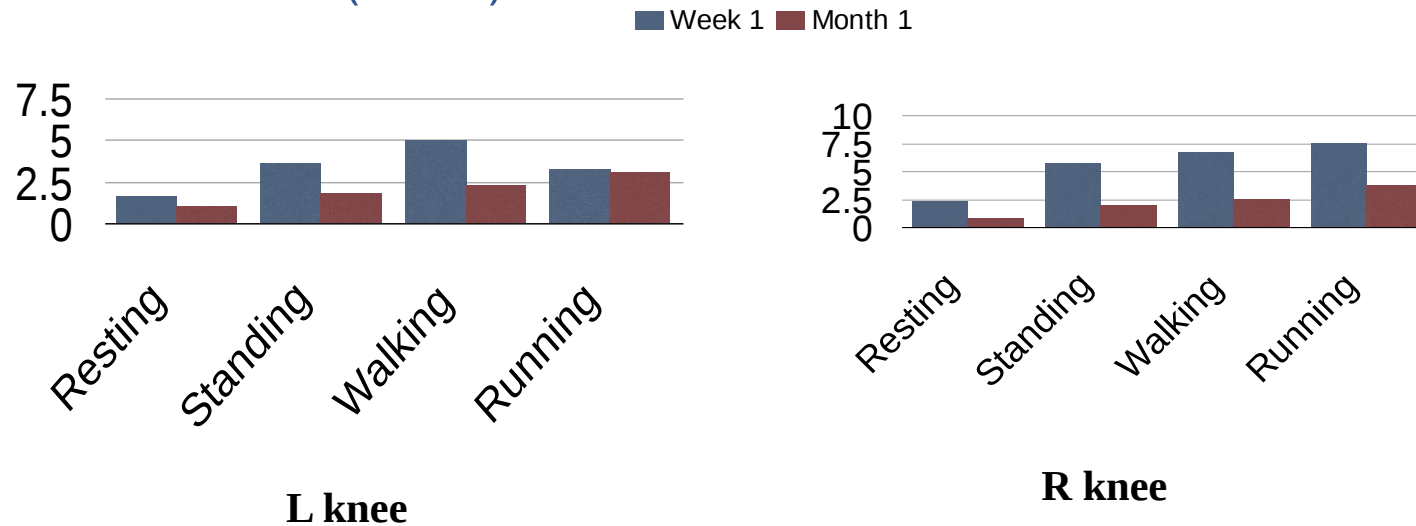
Womac Scores

Western Ontario and McMaster Universities Arthritis Index



CSCTC Assessment Questionnaire

California Stem Cell Treatment Centre Assessment Questionnaire
Rated 0-10 (worst)



Stem cells in osteoarthritis

Osteoarthritis and Stem Cells

OA hurts → less active → put on weight



High blood pressure, diabetes, heart disease, depression,
increased mortality

(Refs: Rosenmann et al 2008, Blair et al 1999, Paffenbarger 1993.)

OA over 60yrs age

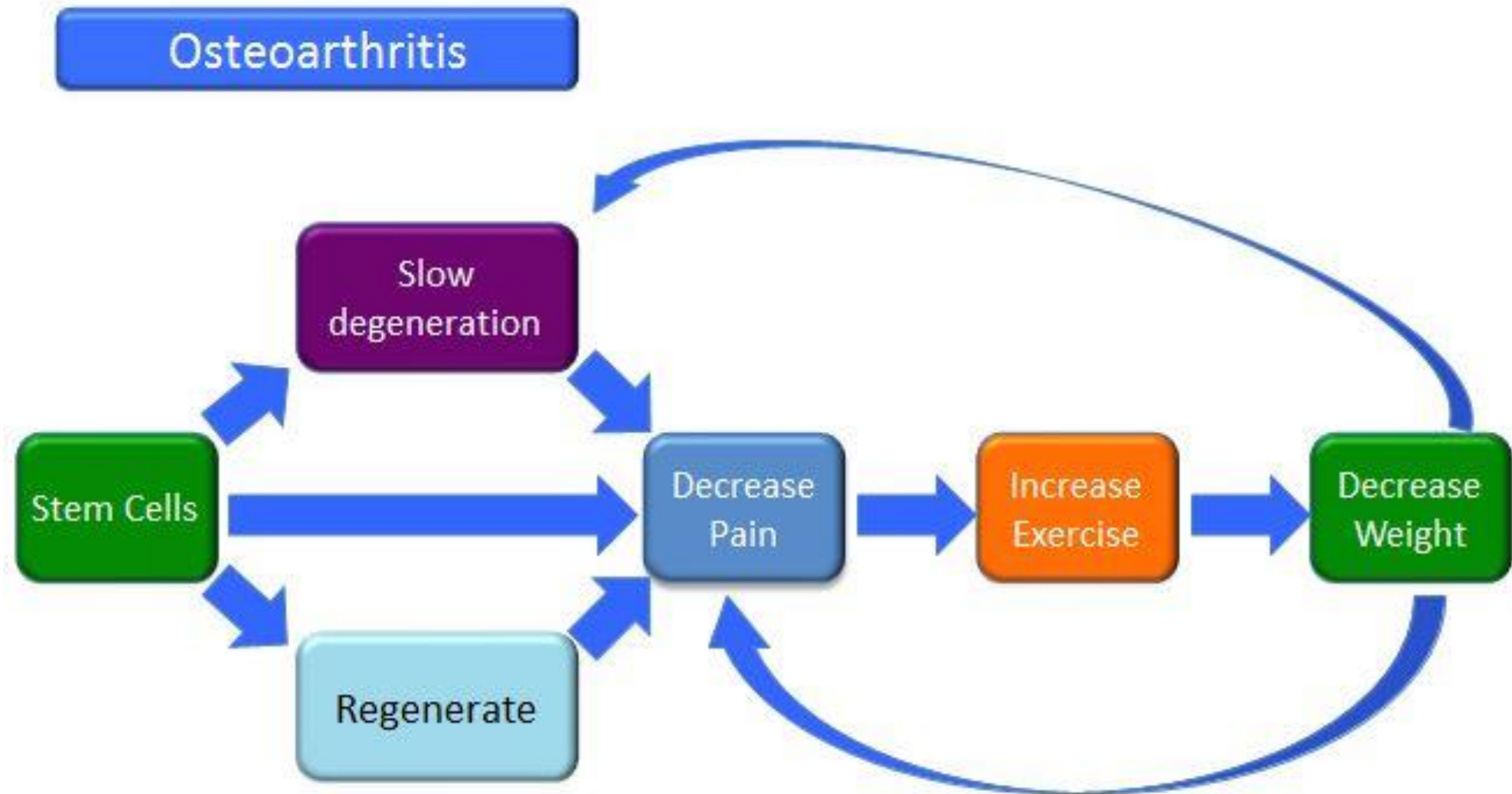
Men 9.6% Women 18% internationally have OA

200 Million with OA by 2050

In NZ 530,000 live with OA
15% population > 15yrs age
650,000 by 2050

NZ Cost \$3.2 billion in 2010

(Ref: <http://bit.do/ArthritisNZ-2010>)





Summary Positive Effects in OA

Evidence to support:

- ✓ Decrease in pain
- ✓ Decreased progression to joint replacement
- ✓ Slow degeneration post menisectomy & OA
- ✓ Possibly regenerate cartilage in OA

Cardio-Pulmonary

- End Stage CHF
- Ischaemic Cardiomyopathy
- Acute MI
- Asthma and Restrictive Lung Disease
- COPD/EMPHYSEMA
- Not Pulmonary Fibrosis

Autoimmune

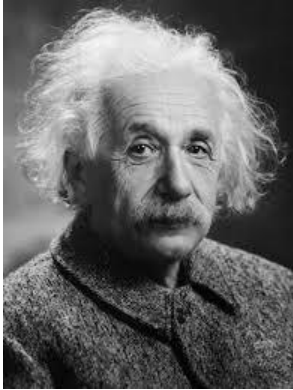
- Fibromyalgia and Scleroderma
- Polychondritis, & Relapsing Polychondritis
- Myasthenia Gravis
- Rheumatoid Arthritis
- Crohns Disease
- Autoimmune Hepatitis
- Alopecia Areata
- Optic Neuritis

Urology

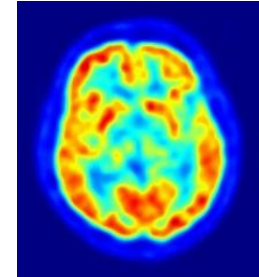
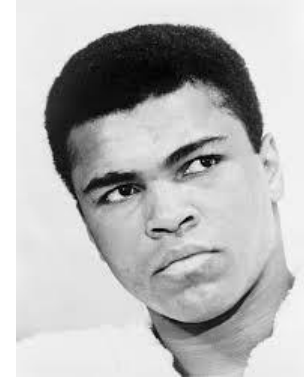
- Interstitial Cystitis
- Peyronies Disease
- Post prostatectomy Incontinence - periurethral, intra-sphincteric fat/SVF
- Erectile Dysfunction

Ophthalmology

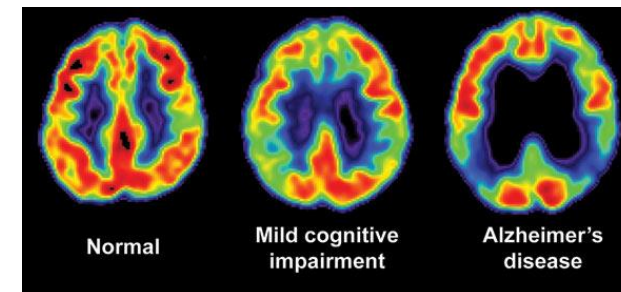
- Retinitis pigmentosa
- Dry Macular Degeneration
- Sjogrens Syndrome - dry eyes, mouth
- Glaucoma



Neurology



- Alzheimer's and Mild Cognitive Impairment
- Strokes, Brain Injury
- Spinal Cord Partial Injuries
- Parkinsons
- Multiple Sclerosis
- Muscular Dystrophy
- ALS
- Neuropathy



Cosmetic Surgery

- ✓ Improved fat grafts scars, breasts, face
- ✓ Improved skin
- ✓ Delay Aging



What Can Go Wrong?

- **Harvest site** : bruising, mild pain, serous ooze, haematoma, infection
- **Systemic** : possible infection, but no rejection
- **Efficacy** : may not work.

Adverse Events

- >6000 cases since July 2010 (CSN)
- PE x1; Nil infections
- **No serious injury (human & animal studies)**
- Int. Stem Cell Society (ISCS) - >1000 reported cases
 - < 2% complications of any kind
 - No serious adverse events



How many SC treatments are required?

- 1 treatment usual
- Neurodegenerative and autoimmune - series

Who Are Not Candidates for SVF Therapy?

- Active Cancer
- Active Infection
- Anticoagulation (relative)

Cellular Surgical Network, CSN

International research sharing protocols/database – USA, Asia, Canada, NZ

High numbers fresh autologous cells for degenerative conditions

Standardized multispecialty care

Advanced deployment methods

Quality Stem Cell Therapy should be available everywhere, easily accessible



Safety of SVF- Stem Cell Therapy

Level 1 evidence “that intra-articular and IV administration of stem cell therapy is safe.”

Australia: Biologic exemption:-

“Autologous MSCs can be used for a single indication, single treatment course under the supervision of a medical practitioner”

Mayo Clinic

“Regenerative medicine is a game-changing area of medicine with the potential to fully heal damaged tissues and organs, offering solutions and hope for people who have conditions that today are beyond repair.”

Penicillin was just mouldy bread once



EDUCATIONAL WEBSITES

www.stemcellrevolution.com

www.stemcell.co.nz

Your Stem Cells - Your Health - Your Life



NZ Stem Cell Treatment Centre

Confidential Appointments

Northland – Queenstown - Orewa - Rotorua

SKIN & VEIN CLINIC

Skin and Vein Clinic, Whangarei