# Cell Assisted Autologous Fat Transfer: The Use of Adipose Derived Mesenchymal Stem Cells and their Importance in Fat Graft Survival

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# Disclosures

- Grants and Speaker's Bureau for
  - Sciton

# History of Fat Transfer

- 1893: Gustav Neuber reports on fat grafting in plastic surgery literature
- 1895: Vincent Czerny transfers lipoma from buttock to breast to replace missing gland
- 1910: Eugene Hollander publishes first report of fat injection in history of plastic surgery
- 1919: Erich Lexer publishes Free Transplantations, a two-volume textbook that devotes nearly 300 pages to fat grafting with wide range of clinical applications

Coleman SR, Mazzol RE, editors. Fat Injection From Filling to Regeneration. St. Louis: Quality Medical Publishing, 2009. p. xxxv.

# History of Fat Transfer

- 1920: Alessandro Pennisi publishes Fat Grafts in Surgery first book entirely devoted to fat grafting
- 1950: Lyndon Peer conducts first scientific studies on fat graft survival
- 1980: Pierre Fournier and Yves-Gerard Illouz develop liposuction, making fat transfer a popular adjunct procedure

Coleman SR, Mazzol RE, editors. Fat Injection From Filling to Regeneration. St. Louis: Quality Medical Publishing, 2009. p. xxxv.

# History of Fat Transfer

- 1997: Sidney Coleman formalizes steps of fat transfer procedure
- 2001 Zuk et al demonstrate that fat tissue contains stem cells (ADSC)
- 2007: Rigotti et al first publication on therapeutic effects of ADSC (regenerative medicine) for treatment of radiation tissue damage

Coleman SR, Mazzol RE, editors. Fat Injection From Filling to Regeneration. St. Louis: Quality Medical Publishing, 2009. p. xxxv.

# Autologous Fat Transfer

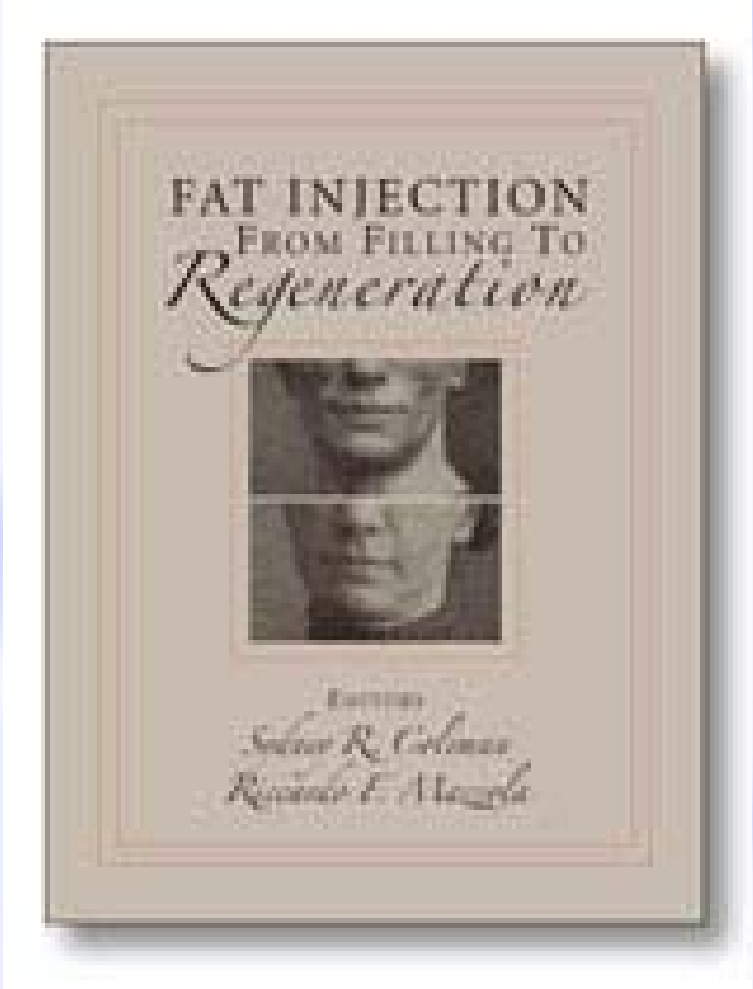
- A review of the literature to date reveals unpredictability of graft retention with the average reported as 50% at two years

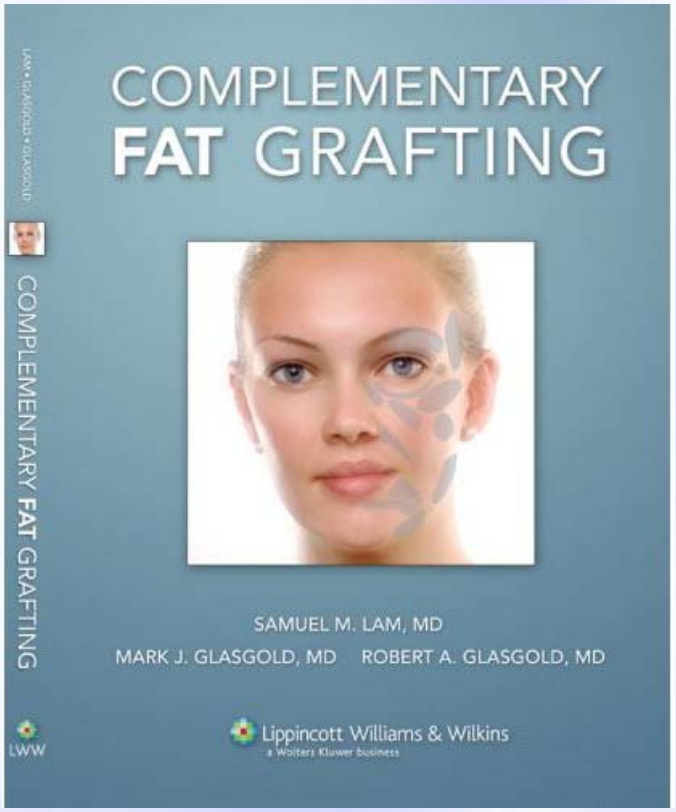
Sadick, Neil in Liposuction and Fat Transfer, Rhoda Narins ed., 2003 Marcel Dekker Inc., New York. Chapter 32 Fat Viability Studies

# Autologous Fat Transfer

- A lack of consensus on a standardized method for optimal harvesting and transplant for graft survival has been partially responsible for unpredictability

# European Masters


FAT INJECTION
FROM FILLING TO
Regeneration


COMPLEMENTARY
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SAMUEL M. LAM, MD
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# Patient Satisfaction

- Autologous fat transfer national consensus survey of 650 ASAPS members evaluating success reported to the practitioner by patients
  - Patient's perception of short-term results 80% good to excellent rating
  - Patient's perception of long-term results 80% fair rating/20% poor

Kaufman MR et al. Autologous fat transfer national consensus survey: trends in techniques for harvest, preparation, application, and perception of short- and long-term results. Plast Reconstr Surg 2007;119(1):323-331.

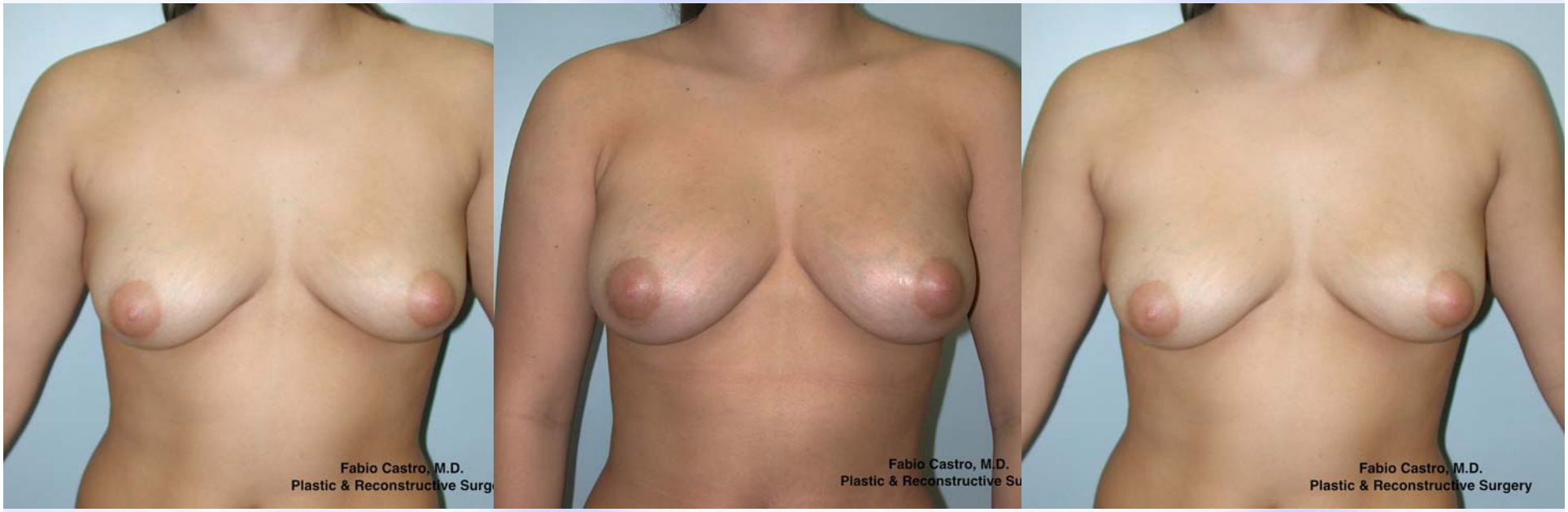
# Market Conditions Inspiring Increased Interest in Fat Transfer

- Increased number of liposuction procedures (2nd most popular surgical procedure, ASAPS 2009 Procedural Statistics)
- Trend toward revolumization of the face, breast, buttocks to restore youthful and high estrogenic appearance
- The discovery of adipose derived regenerative stem cells and their potential
- ASPS position on lipotransfer for breast augmentaion

# The Concern

- The media and commercial vendors have created the buzz
  - "Fat is the new filler"
  - "Liquid gold"

# The Concern




Before

Six Months

One Year

# Possible Outcomes with Lipografting

- Survival theory
  - Fat graft retention depends on the ability of exogenous adipocytes to remain viable upon transfer
  - Nonviable biofilling agent creating a temporary increase in volume and a reactive fibrosis
- Host replacement theory
  - Exogenous ADRC create niche environment that signals differentiation of endogenous preadipocytes to adipocytes with neovascularization and increased fat

# Optimize Autologous Fat Transfer

- Standardize Harvesting Technique
- Standardize Injection Technique
- Implement Cell Assisted Lipotransfer

# Stem Cells from Adipose Tissue

- Possibility of minimally invasive autologous transplant
  - Can be injected immediately following removal
  - Procedure can be performed in office-based setting under local anesthesia
- Cell expansion not necessary
  - Injecting lipoaspirate which has been supplemented with autologous adipose-derived stem cells produces better graft viability

Rigotti G, Marchi A, Sbarti A. Adipose-Derived Mesenchymal Stem Cells: Past, Present, and Future. Aesth Plast Surger (2009) 33:271-273.

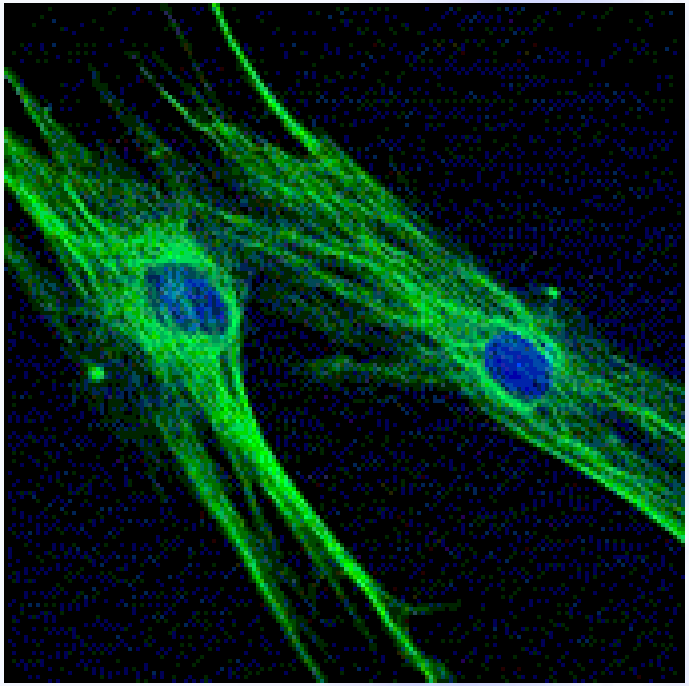
# Stem Cells from Adipose Tissue

- Age not a barrier
  - Adipose stem cells abundant in all stages of life
  - Adipose tissue readily available source

Rigotti G, Marchi A, Sbarti A. Adipose-Derived Mesenchymal Stem Cells: Past, Present, and Future. Aesth Plast Surger (2009) 33:271-273.

# Fat as Regenerative Agent

- Action of injected fat attributed to mesenchymal stem cells
- Mesenchymal stem cells have angiogenic, antifibrotic, and anti-inflammatory effects
- Effects results of release of growth factors
- Anti-inflammatory effect on immune response causes reduction of T-lymphocyte activity



Caplan AI, Dennis JE (2006) Mesenchymal stem cells as trophic mediators. J Cell Biochem 98(5):1076-1084.

# Stem Cell Niche

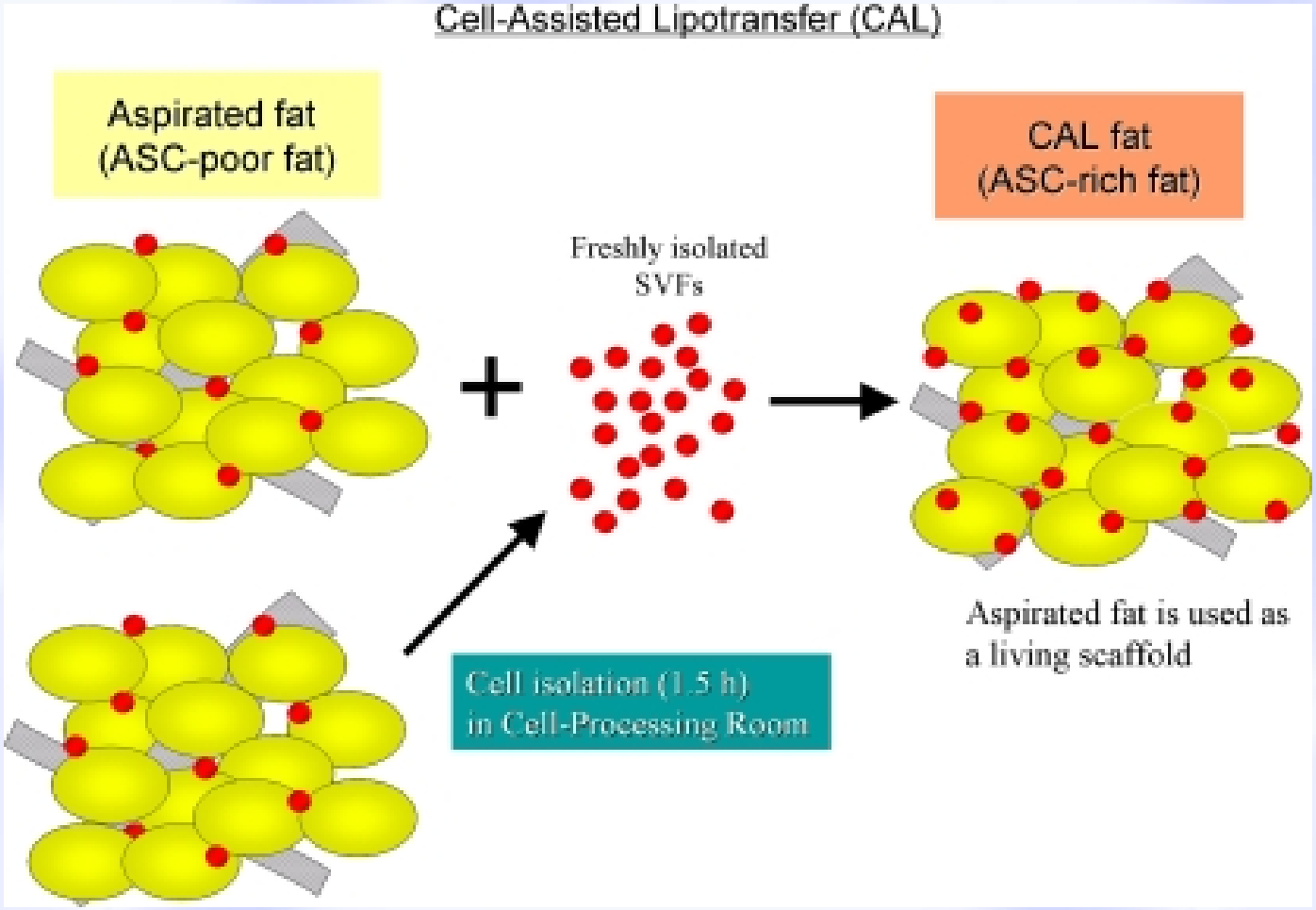
- Made up of stem cell and surrounding system of structures capable of regulating differentiation and tissue development
- Therapeutic target is reconstruction of autologous niches by transferring them from areas of abundance to areas of scarcity

Scadden DT (2006) The stem-cell niche as an entity of action Nature 441: 1075-1079.

# Cell Assisted Lipotransfer (CAL)

- Autologous Adipose Regenerative  Stem Cells are used in combination with lipoaspirate
- Half volume of aspirated fat processed for isolation of stromal vascular fraction (SVF), which contains adipose derived stem cells, endothelial progenitor cells, smooth muscle cells, preadipocytes, and fibroblasts
- Other half of fat is prepared for grafting
- Fat and SVF combined, and injected into target sites

# Cell-Assisted LipoTransfer



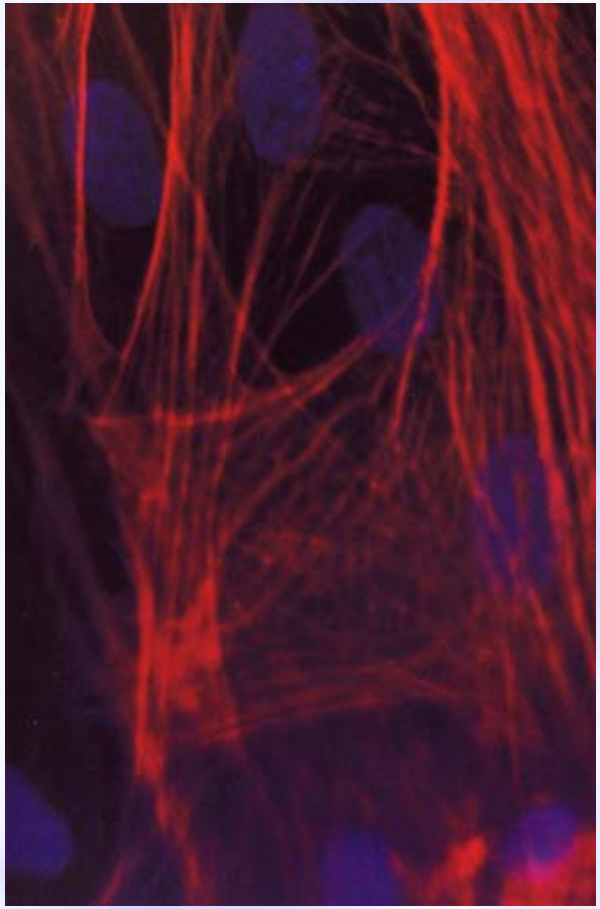
# Cell Assisted LipoTransfer Benefits

- Preadipocytes differentiate into adipocytes, contributing to adipocyte regeneration
- Endothelial progenitor cells differentiate into endothelial cells and vascular cells, resulting in angiogenesis and graft survival
- Release angiogenic growth factors, which influence host tissue
- Survive as adipose-derived stem cells

Yoshimura K et al (2006) Cell assisted lipotransfer: Supportive use of human adipose-derived cells for soft tissue augmentation with lipoinjection. Tissue Eng 12:3375-3382.

# Cell Assisted Lipotransfer Benefits

- Secrete adipokines/growth factors
- Decrease apoptosis
- Decrease inflammation
- Increase preadipocyte differentiation
- Increase angiogenesis
- Improve the niche environment



# Cell Assisted LipoTransfer Benefits

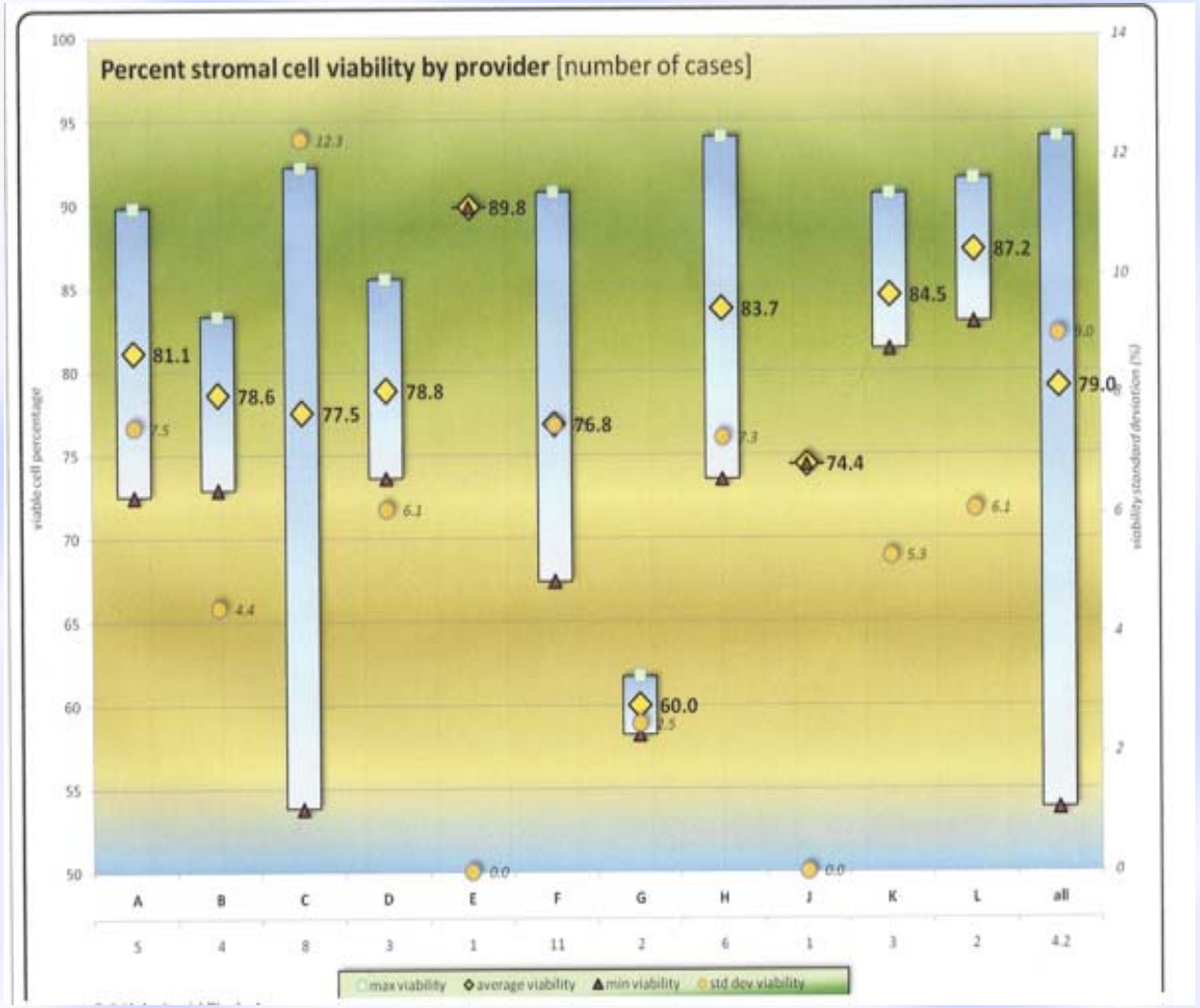
- Regeneration of skin
  - Ability to treat telangiectasia, pigment
- Differentiation of cells means they become specialized based on placement
  - Bone-bone
  - Fat-fat
- Graft ages with host resulting in natural, long lasting result

# Harvesting Techniques affect Viability of Adipocytes and ADRCs

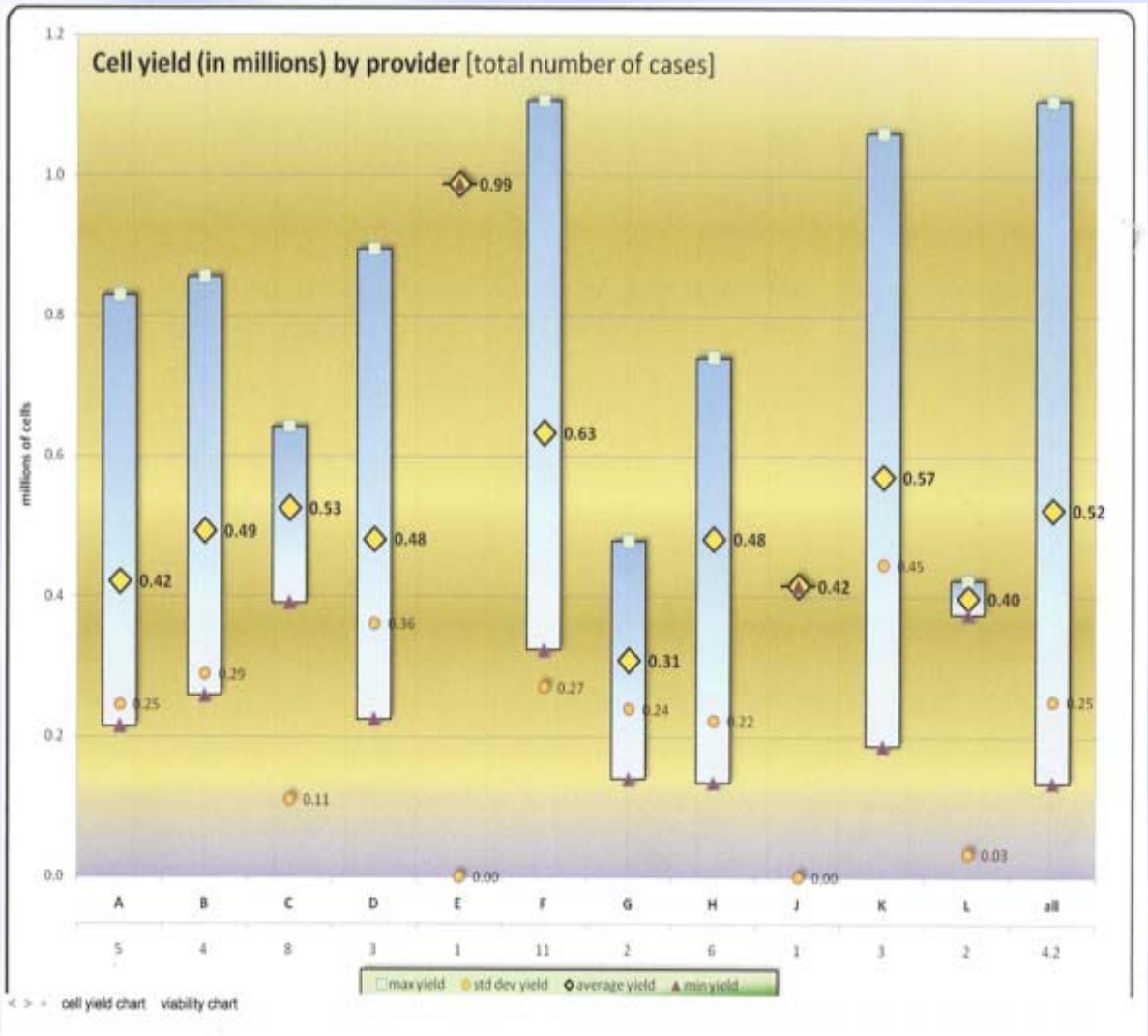
- Traditional Suction Assisted Liposuction (SAL)
- Power Assisted Liposuction (PAL)
- Ultrasound Assisted Liposuction (UAL)
- Laser Assisted Liposuction (LAL)

- Water Assisted Liposuction (WAL)
- Specialized devices (Lipivage, Aquavage, new low pressure Tumi syringes)

# Stem Cell Viability



# Stem Cell Yield



# Variables That Matter

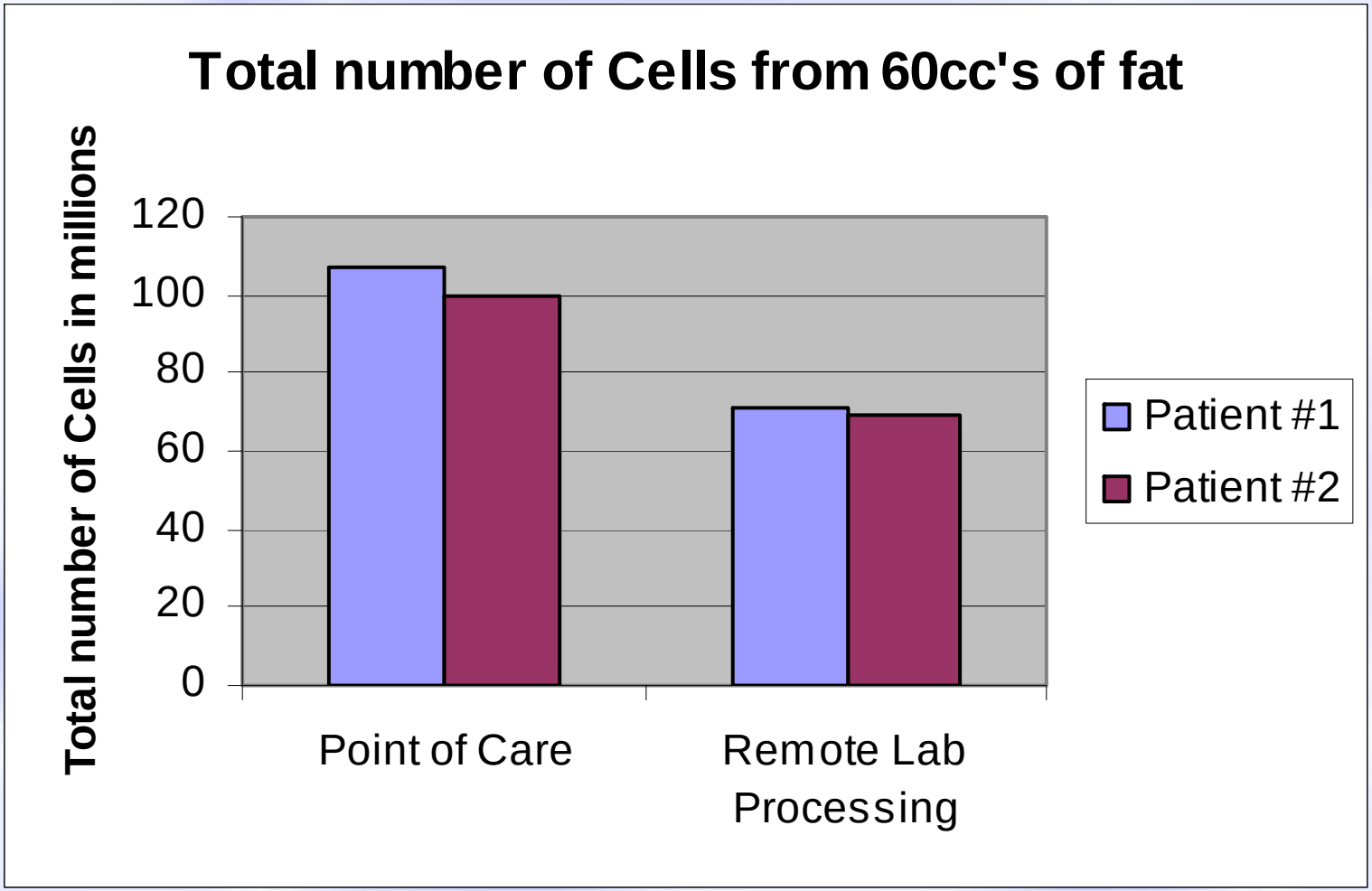
- Blunt cannula
- Cannula size
- Closed system
- Tumescent anesthesia
- Washing the cells?
- Decantation vs. Centrifuge?
- Micrograft technique vs. bolus technique
- Injection into multiple layers
- Total volumes injected
- Frozen specimens

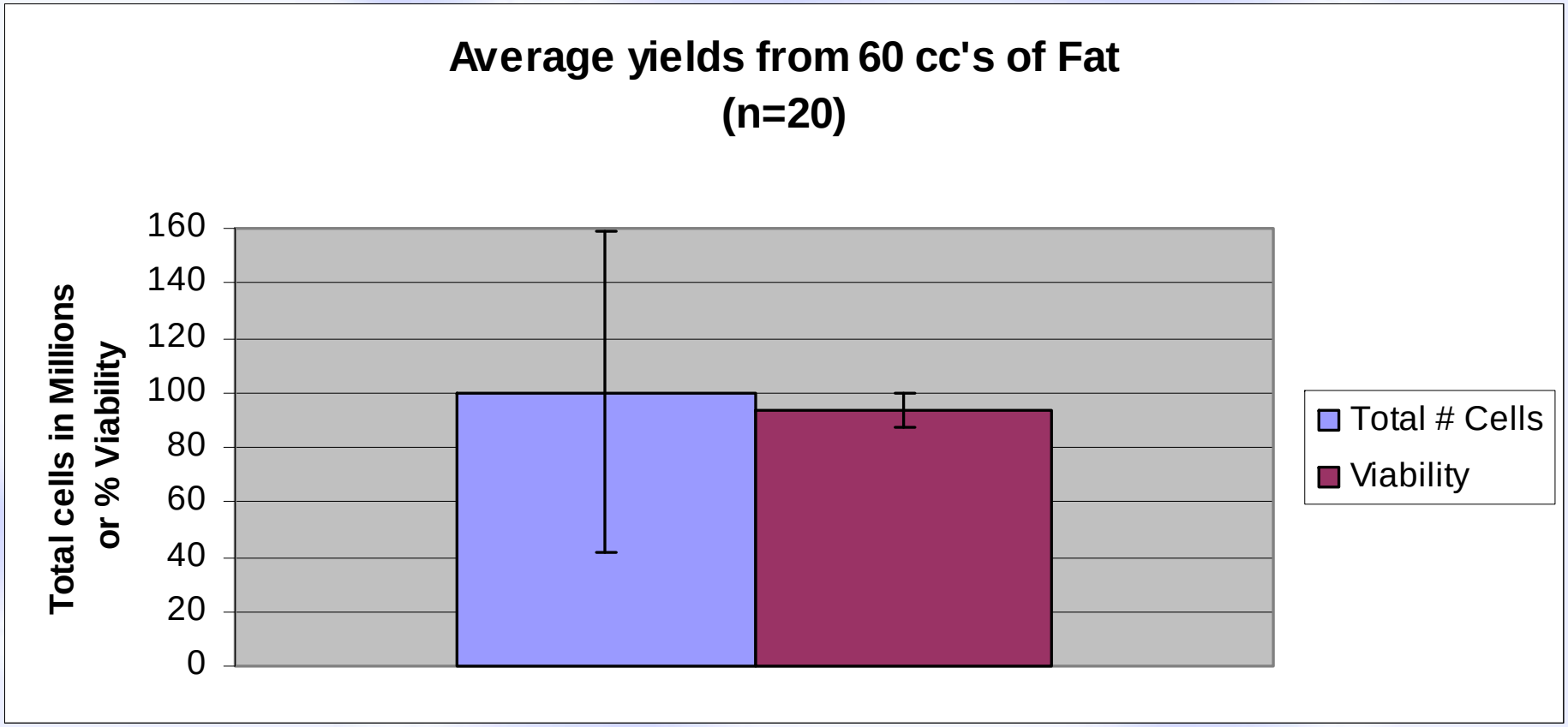
McCurdy JA Jr. Five years of experience using fat for leg contouring (commentary). Am J Cosmet Surg 1995;12:228.

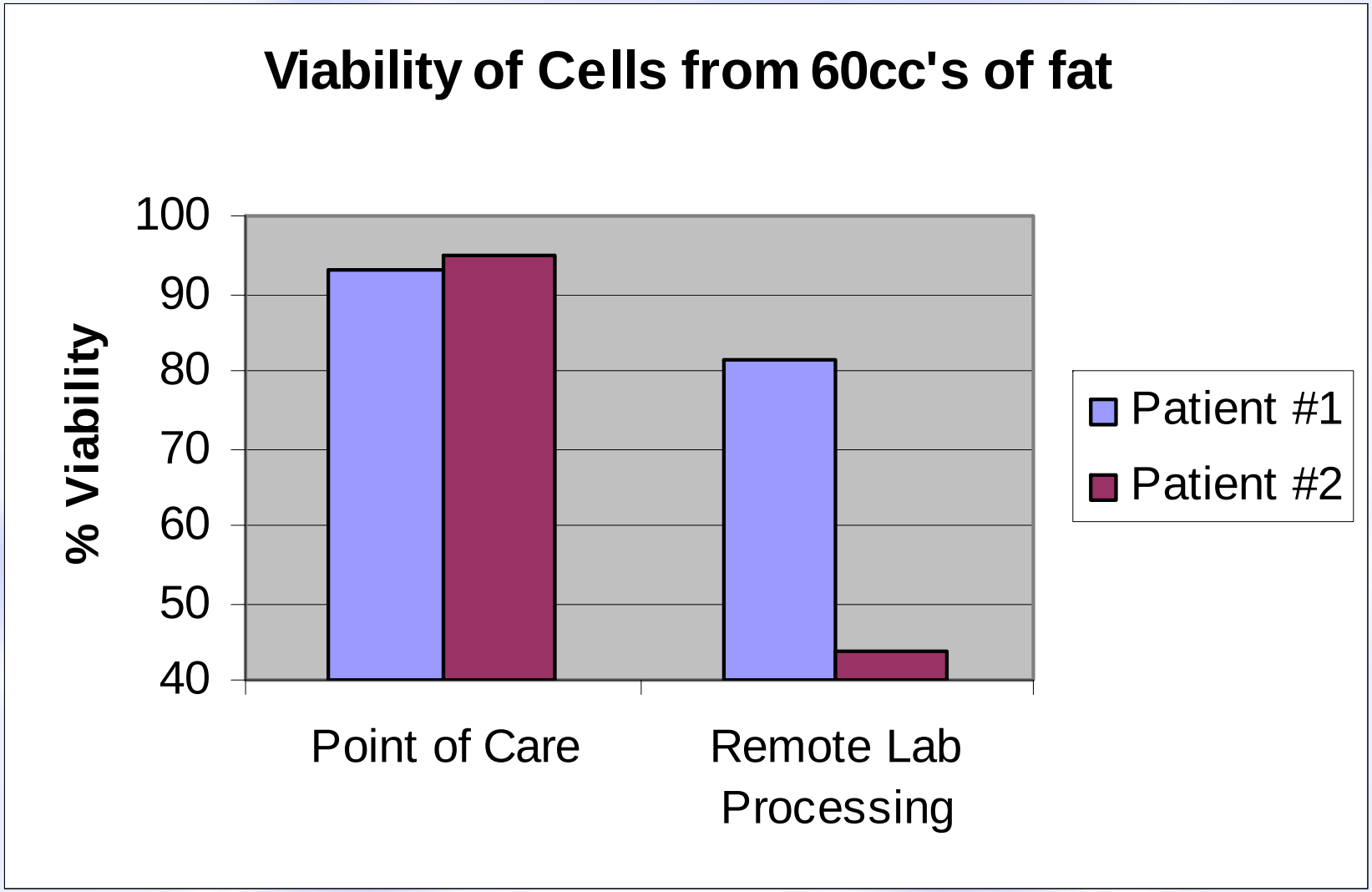
# CAL Survival Studies

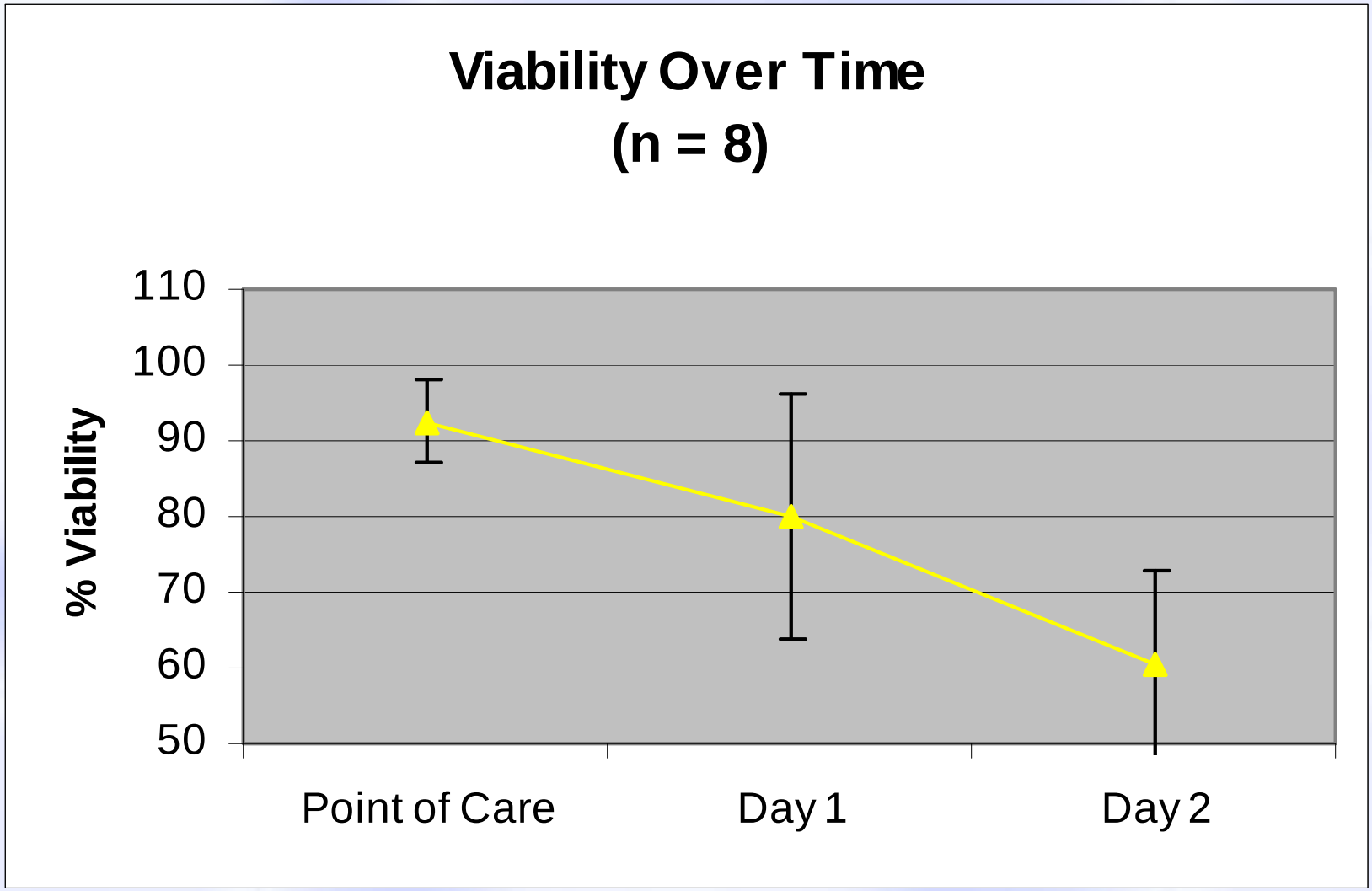
- Matsumoto et al
- 35 % greater graft survival measured by volume when ADSC were added measured at 6 months
- Transplanted cells expressed vascular endothelial cell markers

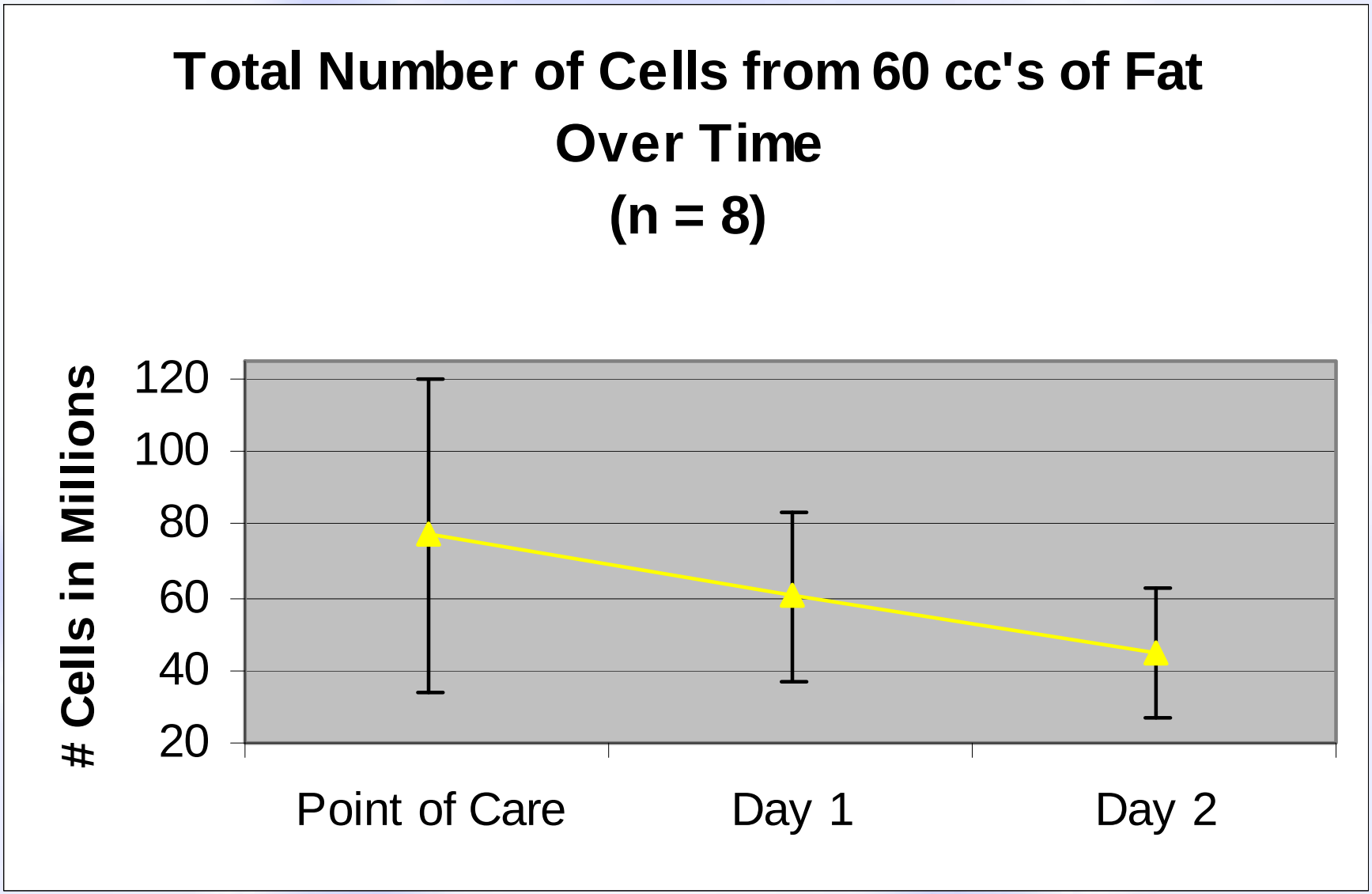
Matsumoto D et al. Cell-assisted lipotransfer: supportive use of human adipose-derived cells for soft tissue augmentation with lipoinjection. Tissue Eng 2006;12:3375-3382.


Total number of Cells from 60cc's of fat
Total number of Cells in millions
120
100
80
60
40
20
0
Point of Care
Remote Lab Processing
Patient #1
Patient #2


Average yields from 60 cc's of Fat
(n=20)
Total cells in Millions
or % Viability
160
140
120
100
80
60
40
20
0
Total # Cells
Viability


Viability of Cells from 60cc's of fat
% Viability
100
90
80
70
60
50
40
Point of Care
Remote Lab Processing
Patient #1
Patient #2


Viability Over Time
(n = 8)
% Viability
110
100
90
80
70
60
50
Point of Care
Day 1
Day 2


Total Number of Cells from 60 cc's of Fat
Over Time
(n = 8)
# Cells in Millions
120
100
80
60
40
20
Point of Care
Day 1
Day 2

# Cell Isolation Technique

- Validated procedure via reproducibility and robustness analysis – process consistently produces pre-determined acceptance criteria
- Yields 500,000-1,000,000 ADRCs per gm of fat which is higher than the automated methods
- Requires 70 minutes of tech time

# Regulatory Issues

- Technique for obtaining stem cells adheres to current code of federal regulations for use in physicians practices:
  - Minimally manipulated
  - Homologous use
  - Autologous use
  - Administered by a physician in his/her medical practice at point of care
  - CFR 1271 and PHA 351 and 361

# Patient Results from 60cc Fat

| Test | 1A | 2A | 2B | 3A | 3B |
|---|---|---|---|---|---|
| Cell Count | 61.7e6 | 46.6e6 | 45.4e6 | 65.7e6 | 69.9e6 |
| Viability | 100% | 100% | 100% | 99% | 100% |
| CD34 | 72% | 52.3% | 68% | 64.1% | 51.2% |
| Sterility | No Growth | No Growth | No Growth | No Growth | No Growth |
| Endotoxin (EU/ml) | <0.5 | <0.5 | 1.1 | 3.51 | <3 |

# ADRC Isolation Method

- Can be implemented in your offices today
- Will help optimize Autologous fat grafting and give patients more reliable and reproducible results
- Have the added benefit of providing skin rejuvenation in the treatment area

# Cell-Assisted Facial Fat Transfer

# Indications for LipoFilling

- Facial volume loss
- Tear trough deformity
- Jowling
- Submalar hollowing

# Contraindications for LipoFilling

- Skin laxity
- Deep nasolabial folds
- Cheek ptosis
- Neck ptosis
- Cancer
- Cardiovascular disease
- DVT/pulmonary embolus
- Heavy smoker

# Patient Selection

- Facial volume loss
- Adequate skin laxity
- 35-60 years of age
- Understands downtime and procedural process

# LipoFilling Treatment

- Consultation
- Pre-operative instructions
- Anesthesia of face and donor site
- Fat harvesting
- Fat processing
- Fat injection
- Post-operative instructions
- Follow-up treatment as needed

# Aging Face


- Scalloping of jawline
- Prominent convexity of temples, lateral cheeks, and suborbital area
- Lips thinned
- Conversion of facial arcs to straight lines
  accounts for excess skin

# Atrophy/Hypertrophy Aging Model

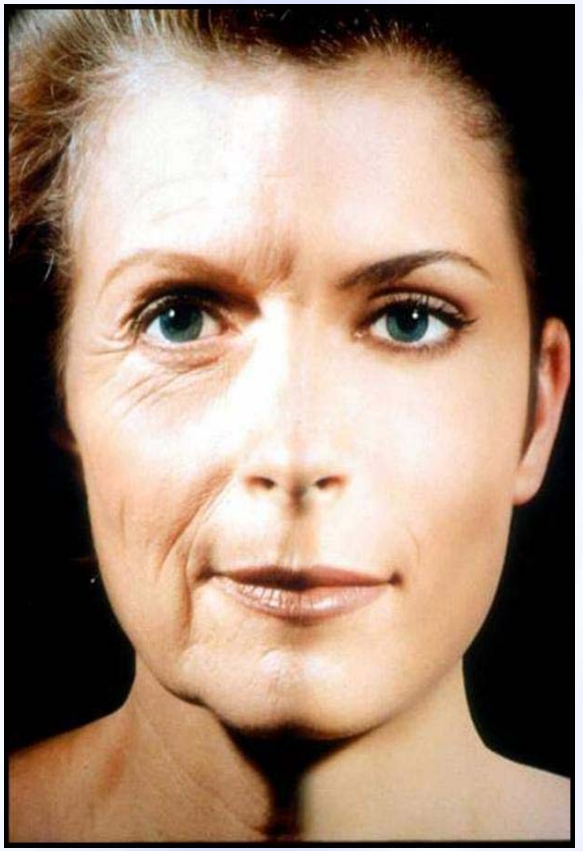
- Fat atrophy occurring in periorbital, forehead, buccal, temporal, perioral areas
- Fat hypertrophy occurs submentally in jowl, lateral nasolabial fold, lateral labiomental crease, and lateral malar areas

# Facial Aging

- Sum of factors acting on four main facial aesthetic components
  - Soft tissue quality
  - Soft tissue quantity
  - Soft tissue dynamics
  - Supporting bony, dental, and cartilaginous skeleton

# Facial Aging: General Considerations

- Face shape becomes longer, narrower
- Face shape shifts from triangular to rectangular shape
- Profile curves flatten
- New curves appear
- Volume depletes
- Profile segments elongate



# Consultation

- Patient should bring facial photo that is 10-20 years old
- Compare with photo taken on consultation day

# Facial Evaluation

- Volume of forehead arc
- Position and fullness of brow
- Fullness of temporal and glabellar areas
- Hollowing of infraorbital area
- Tear trough deformity
- Fullness of malar and cheek area
- Proportion of mid-face
- Buccal hollowing
- Perioral
- Oral commissures

# Facial Profile Analysis

- Projection of lips
- Chin projection
- Mental groove
- Prejowl sulcus
- Mandibular fullness

# Injection Technique

- Requires in-depth knowledge of facial anatomy especially musculature
- Small injection cannulas used
- Infiltrate cannula through 2 mm incision into the proper tissue plane of respective tissue
- Advance cannula to distal aspect of target muscle
- Deposit fat in small amounts in retrograde fashion as cannula is withdrawn.

# Fat Injection Technique

- Blunt insertion of tiny fat deposits placed in multiple anatomic layers
- Small fat deposits permit improved surface to volume contact between surrounding tissue and deposited fat, increasing cell viability

# Fat Injection Technique

- Fat injected into three facial planes
  - Deep:  above periosteum
  - Intermediate:  within muscle, fascia, deep subcutaneous plane
  - Superficial:  medium to superficial subcutaneous plane

# General Injection Quantities

- Malar zone: 4-6 cc
- Nasolabial fold: 2-4 cc
- Melomental fold: 1-2 cc
- Cheek: 4-6 cc
- Glabellar: 2-4 cc
- Temples: 6 cc
- Upper/lower lip: 2.5 cc
- Chin: 8-15 cc

# Post-Treatment Considerations

- Edema and bruising are common
- Perioral muscle soreness
- Continue oral antibiotics
- Sleep with head elevated
- Ice for 5 minute period for three days
- Patient downtime may be from 5-10 days depending on amount and areas injected

# Cell-Assisted Facial Lipotransfer Clinical Study

- Purpose: evaluate efficacy of supplementation of ADSC to adipose grafts for facial implantation
- 6 patients; 3 injected with plain adipose grafts, 3 injected with ADSC supplemented grafts
- All patients experienced improvement, but cell-assisted patients had better clinical improvement score at 9 months post-procedure

Yoshimura K et al. Cell-Assisted Lipotransfer for Facial Lipoatrophy: Efficacy of Clinical Use of Adipse-Derived Stem Cells. Dermatol Surg 2008;34:1178-1185.

# Side Effects & Complications

- Edema
- Ecchymoses
- Infection
- Overcorrection
- Vascular occlusion
- Muscle injury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