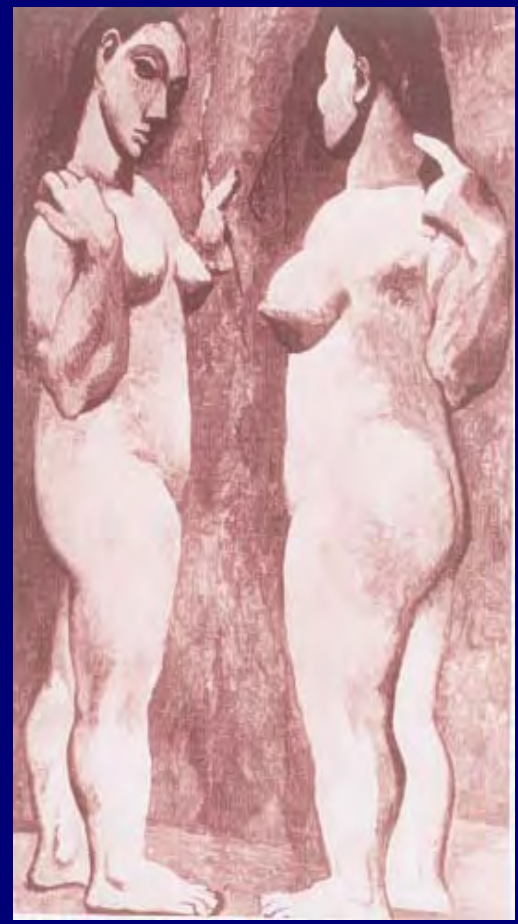
National Cancer Institute

Preoperative Therapy in Invasive Breast Cancer

Reviewing the State of the Science and Exploring New Research Directions

Reconstruction After Preoperative Therapy



Michael J. Miller, M.D.

The Ohio State University
Comprehensive Cancer Center

Arthur G. James Cancer Hospital

Solove Research Institute

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

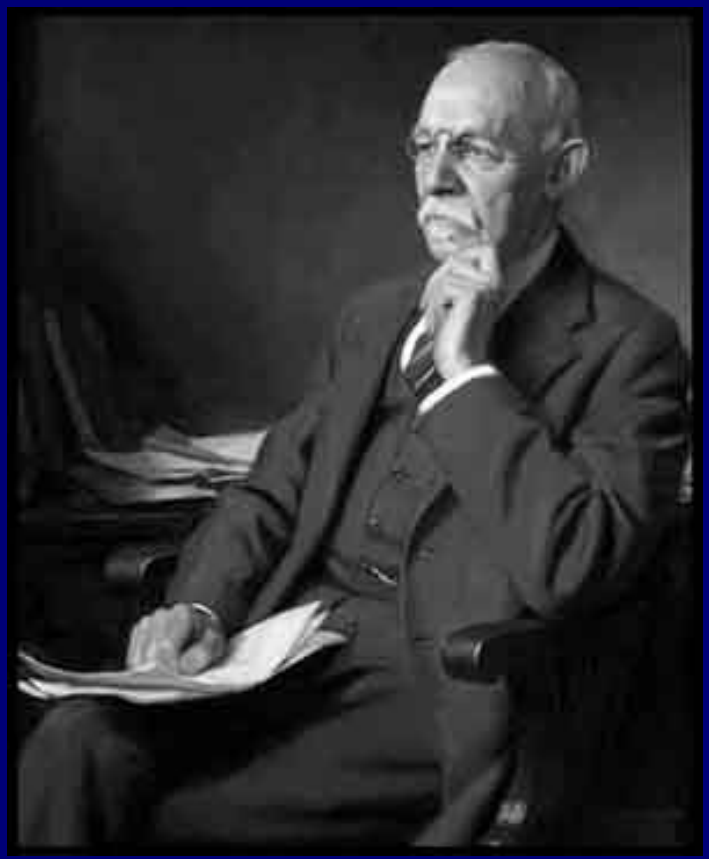
National Institutes of Health

Breast Reconstruction

First report: 1906 Louis Ombredanne (France)

www.urofrance.org

Breast Reconstruction



William Halsted (1852-1922)

- Father of American Surgery
- Vigorously opposed breast reconstruction

Halsted Mastectomy

- Breast Skin
- *Pectoralis Major*
- Axillary contents

Initial Reports- 1980's

- Albo RJ. *Amer J Surg* 140:131-6, 1980.
- Georgiade G. *Ann Plast Surg* 8:20-8, 1982.
  - 62 patients
  - 42% > 2yr F/U
- Georgiade G. *Plast Reconstr Surg* 76:415, 1985.
  - Recon. (n=101) vs. non-recon (n=377) cohorts
  - Median F/U 36 months (92% > 1yr)
- Noone RB. *Plast Reconstr Surg* 76: 258, 1985.
  - 185 patients
  - Mean F/U 26 months (range 2-82)

No adverse affect on disease outcomes

Breast Deformity

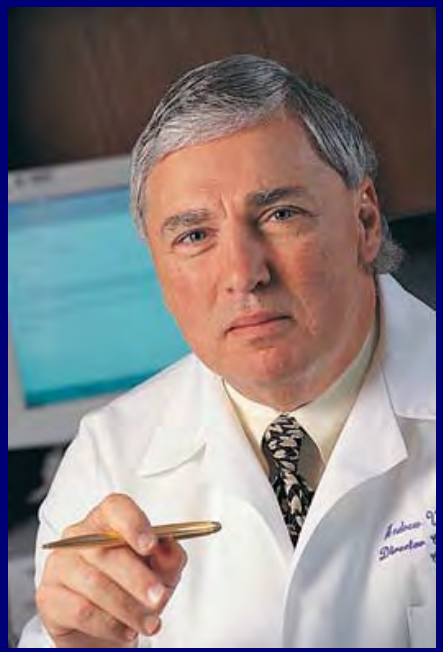
Physical Deformity

Consequences:

- Aesthetic
- Functional
- Emotional
- Social

= *Suffering*

NCI Challenge Goal Initiative



Year 2015

… eliminate *suffering* …
from cancer.

Andrew von Eschenbach, M.D.
Director, National Cancer Institute
Jan. 2002 - Dec. 2006

Paradigm Shift

Eliminate ~~Cancer~~ *Suffering*

Mission accomplished.

Paradigm Shift

Eliminate ~~Cancer~~ *Suffering*

Mission accomplished?

At least one step closer…

Consequences

Therapeutic Goal: Restore Wholeness

Therefore:

- Multidisciplinary care team including reconstructive surgeons.
- More difficult to study.
- Quality of life outcome changes therapeutic risk/benefit calculation

Multidisciplinary Care

Not universally adopted…

- Low overall rate of reconstruction
- Extreme geographic variation
- Knowledge deficit
  - Limited awareness of contemporary methods
  - Skepticism of clinical value

Paulson, 1994; Thompson, 2000; Wanzel, 2002; Morrow, 2001; Polednak, 2000.

Knowledge Deficit: Practitioners

- Wanzel et. al. Reconstructive breast surgery: referring physician knowledge and learning needs. Plast Reconstr Surg 110(6): 1441, 2002.

TABLE II

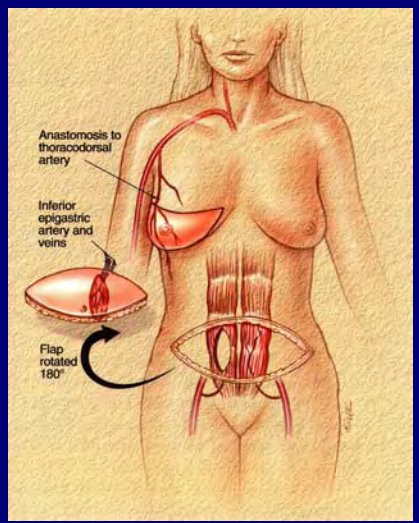
Summary of the Level of Agreement with Statements Concerning Attitudes toward Breast Reconstruction, by Physician Specialty and Gender

Survey Statement: Breast Reconstruction. . .	Physician Specialty (%)*						Physician Gender		
	Oncologists		General Surgeons		Primary Care Physicians		Male (%)	Female (%)	*p* Value
	Yes	No	Yes	No	Yes	No			
Adversely delays detection of local cancer recurrence	36.7	31.1	39.8	51.1	31.5	43.8	37.1	35.2	0.63
Adversely interferes with adjuvant oncologic therapy	38.9	48.9	22.7	59.1	9.7	75.0	24.9	28.0	0.90
Should be offered only to long-term cancer-free survivors	27.8	43.3	11.4	71.6	20.5	60.3	23.6	20.6	0.96
May have a positive effect on quality of life	95.6	1.1	95.5	2.3	94.6	0.0	96.9	92.3	0.39
Is an appropriate use of health-care resources	81.1	3.3	85.2	9.1	71.2	8.2	76.0	84.1	<0.05

* In each case, the remainder of the respondents were "unsure" of their opinion regarding the statement.

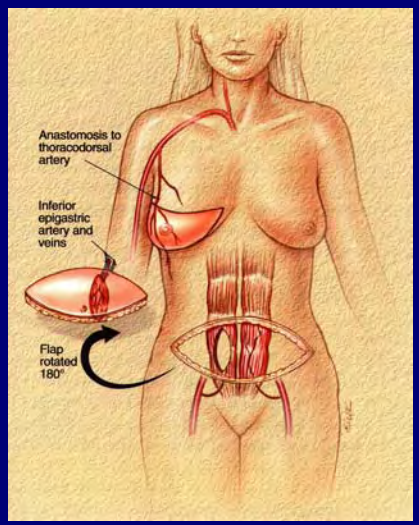
Reconstruction Process

- Deformity
- Op #1 (Immediate)



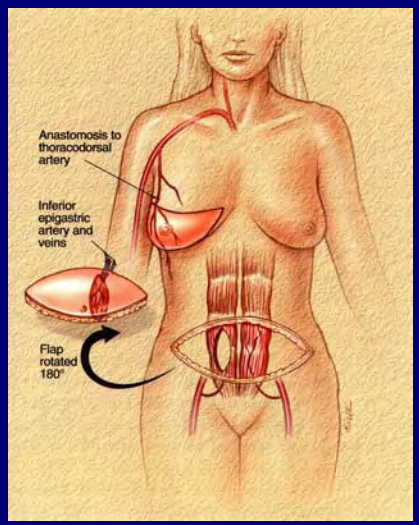
Reconstruction Process

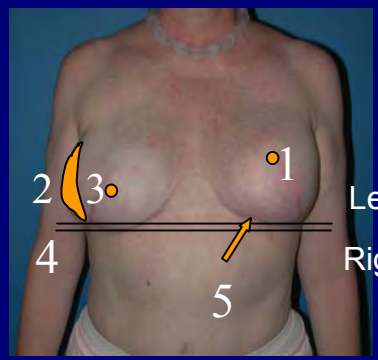
- Deformity
- Op #1 (Immediate)

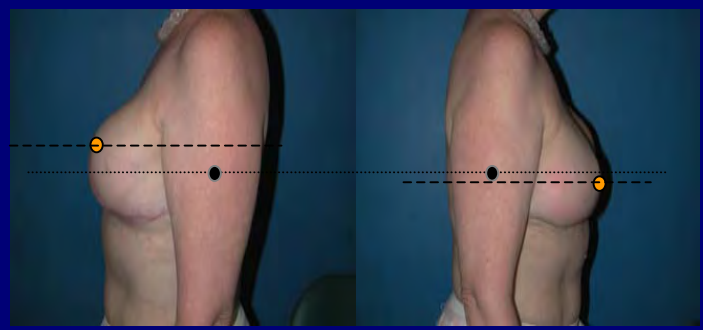


Reconstruction Process

- Deformity
- Op #1 (Immediate)



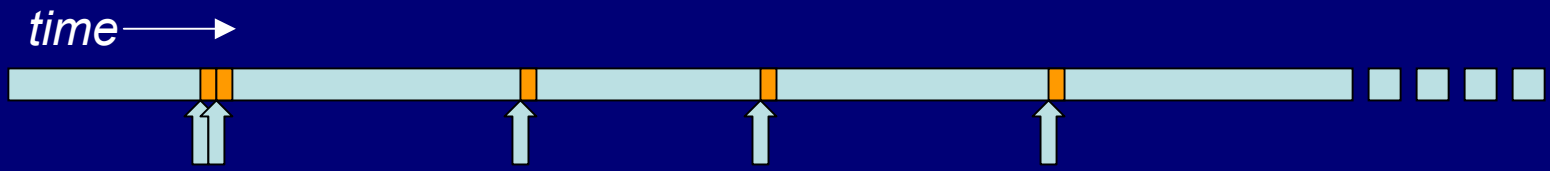




Problem list:

1) Point of maximum projection (anterior)
2) Point of maximum projection (lateral)
3) Breast width
4) IMF position
5) Irregular left IMF

Reconstruction Process

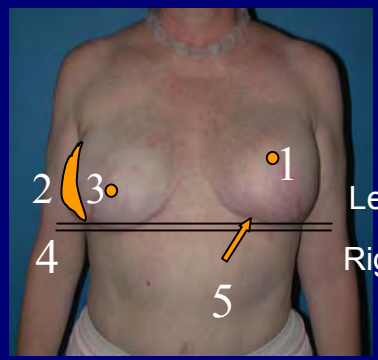


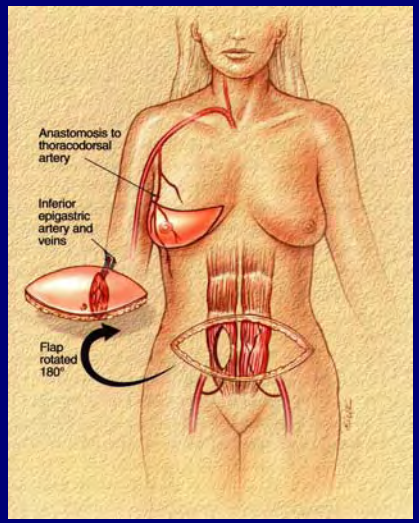
- Deformity
- Op #1 (Immediate)

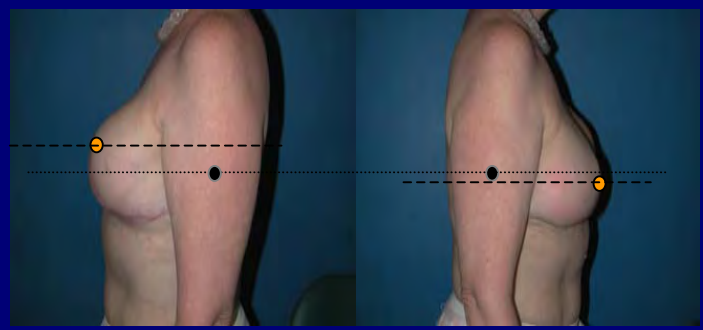
Op. #2

Op. #3

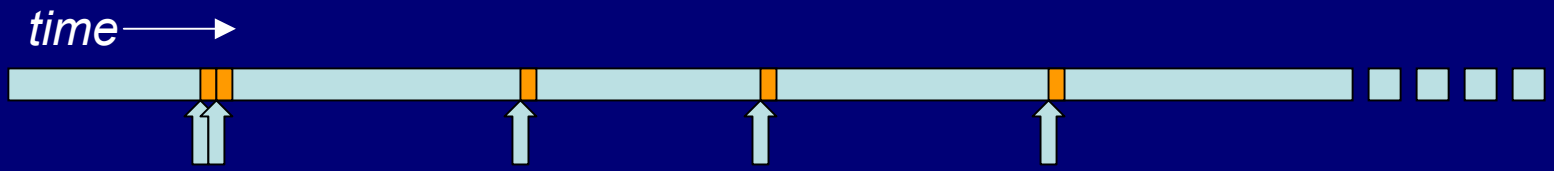
Op. #4







Reconstruction Process



- Deformity
- Op #1 (Immediate)

Op. #2

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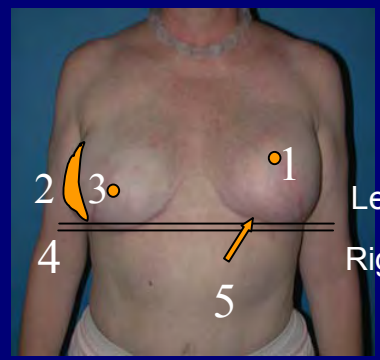
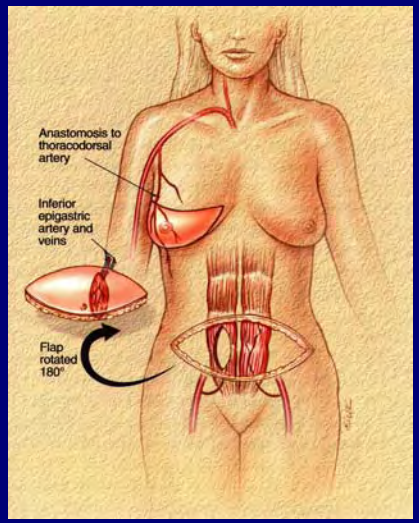
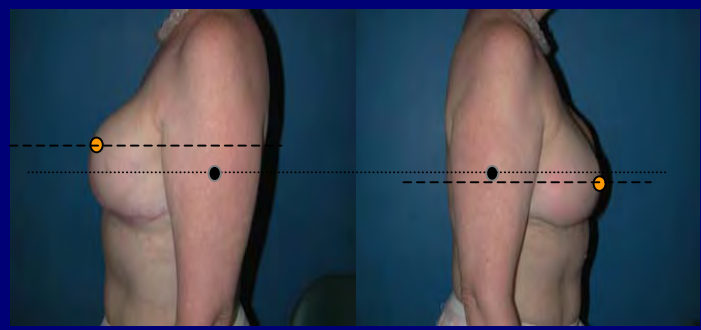






Reconstructive Techniques

Post-mastectomy reconstruction

- Tissue expander/breast implant
- Tissue flap/implant combination
- Autologous tissue flaps
  - Pedicled transfers
  - Free tissue transfers
- Skin-sparing

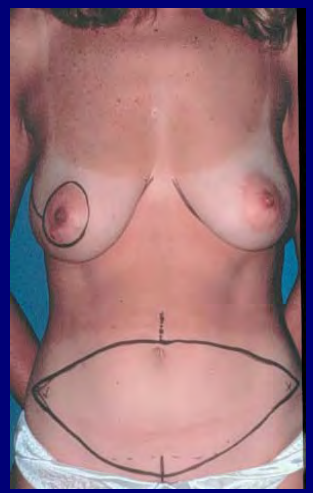
Reconstructive Techniques

Pre-operative

Post-operative

Implant reconstruction

Latissimus Dorsi flap +
Implant reconstruction

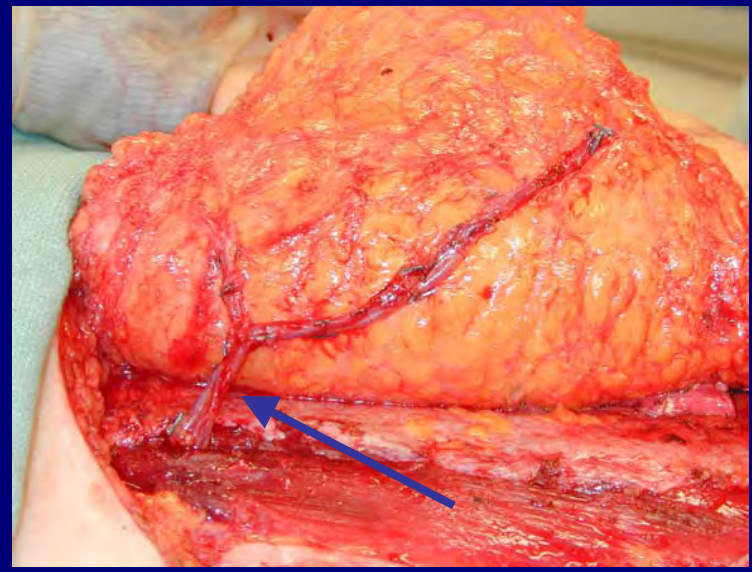


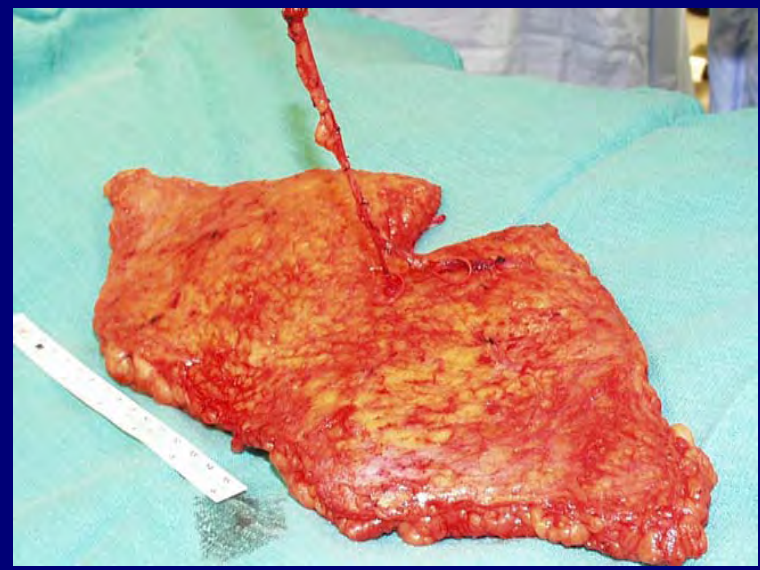
Autologous tissue
reconstruction

Perforator Flaps

DIEP flap

- Advantages
  - Spares Muscle
  - Minimizes Pain
  - Less functional morbidity
- Disadvantages
  - Technical challenge
  - Increased operative time
  - Variations in anatomy
  - Less blood supply

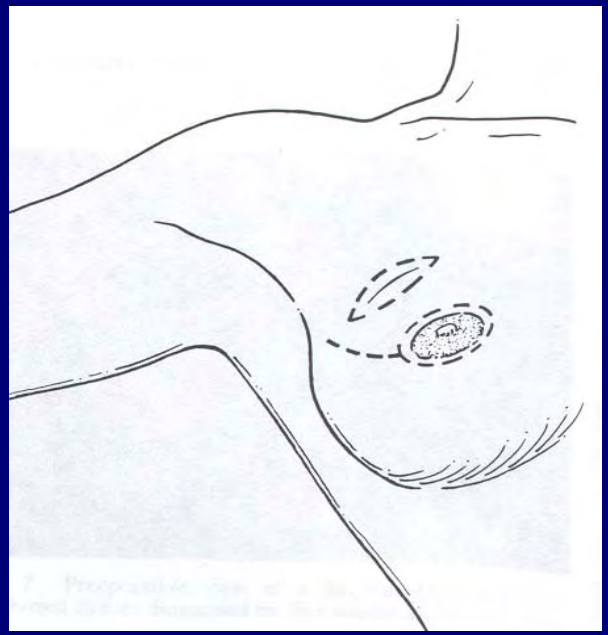


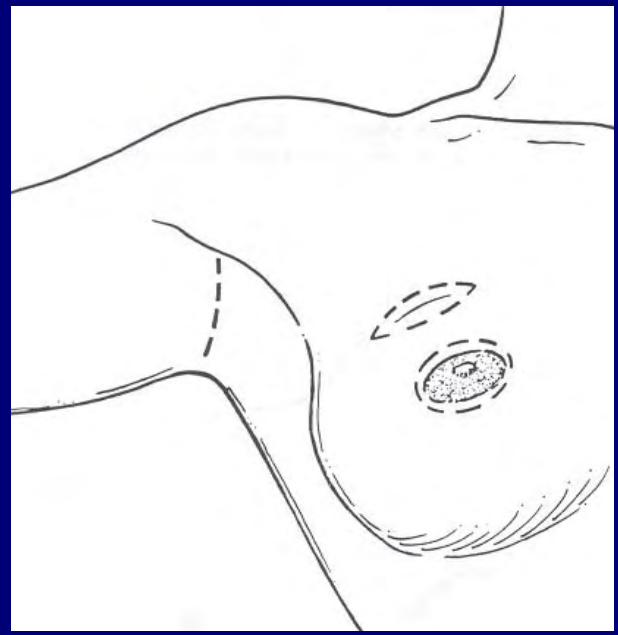


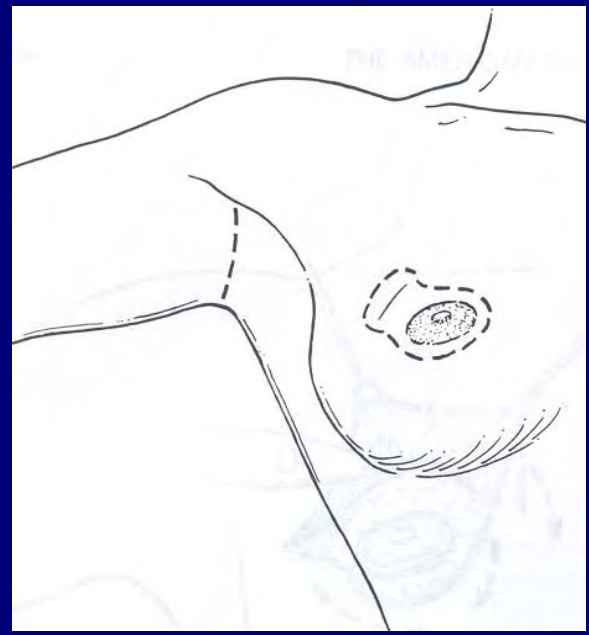
Skin-Sparing Mastectomy

Incisions for:

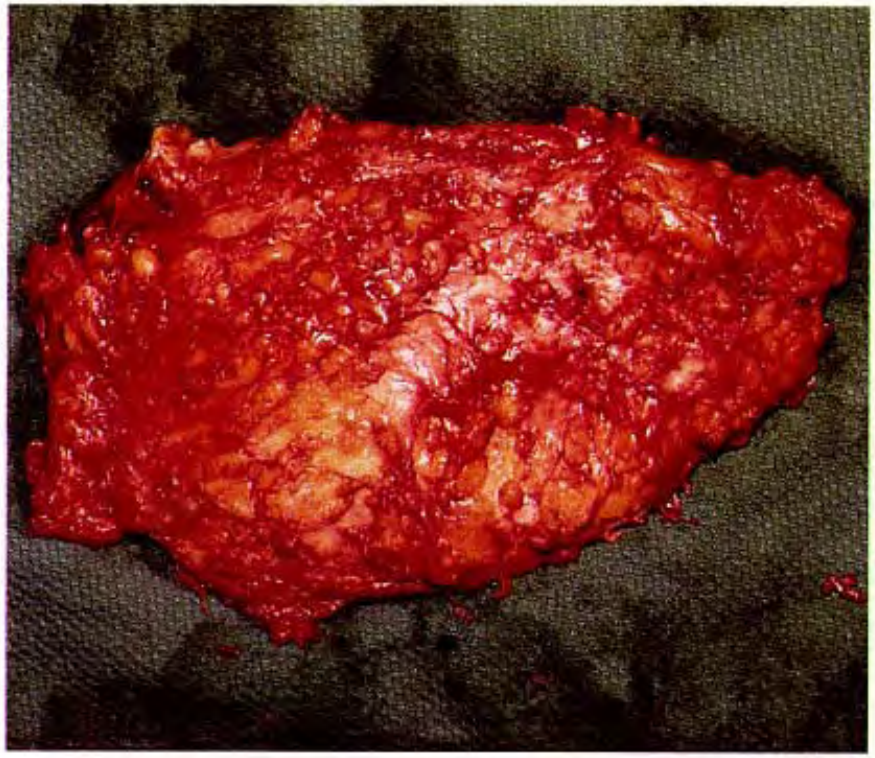
- Nipple and Areola
- Biopsy scars
- Access to the axilla
- Skin areas “at risk”







Skin-Sparing Mastectomy



The *ablative surgeon* begins the reconstruction!

Skin-Sparing Mastectomy

Skin-Sparing Mastectomy

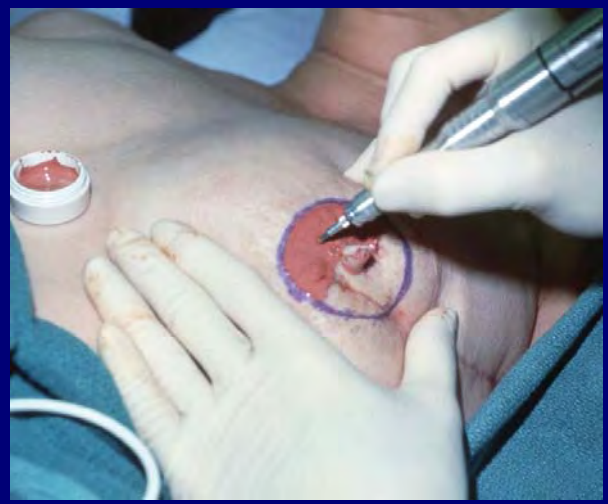
Pre-operative appearance

Post-operative appearance

Nipple/Areolar Reconstruction

Nipple Reconstruction

Areolar Micropigmentation



Overview

- Background
  - Reconstruction and multidisciplinary care
  - Techniques
- Preoperative therapies
  - Chemotherapy
  - Radiotherapy
  - Recurrent disease
- Research opportunities

Pre-operative Chemotherapy

Deutsch MF. *Ann Plast Surg.* 42(3):240-4, 1999.
- 31 TRAM patients
- Increased minor complications
- No effect on resumption of therapy

Selber JC. *Annals of Plastic Surgery.* 56(5):492-7, 2006.
- 500 TRAM patients
- No effect on complications

Mehrara BJ. *Plast Reconstr Surg.* 118(5):1100-9; 2006.
- 1195 TRAM patients
- Increased risk minor complications
- No effect on resumption of therapy

Cordeiro PG. *Plast Reconstr Surg.* 118(4):825-31, 2006.
- 1221 tissue expander/implant patients
- Safe to continue CTx during expansion

Radiotherapy and Reconstruction

Author	RTx Patients	Conclusions
1997 Williams	19	increased “fibrosis”
1998 Zimmerman	21	“cosmetically acceptable”
2000 Hanks	25	“well-tolerated”
2001 Lin	98	increases risk
2002 Proulx	15	“acceptable”
2002 Rogers	30 (matched pairs)	delay reconstruction
2005 McCarthy	12 (bilateral recon unilateral RTx)	↑ capsule, delay RTx
2005 Spear	80	↓ aesthetics, symmetry
2006 Behranwala	44	↑capsule, ↑pain,↓aesth.
2006 Cordiero	136	↑ complications

Radiation Effects on Irradiated versus Untreated Sides in 14 Bilateral TRAM Patients

	Untreated Side (n = 14)		Irradiated Side (n = 14)	
	n	%	n	%
Flap loss	0	0	0	0
Normal breast mound	13	93	2	14
Firm flap	0	0	6	43
Hyperpigmentation	0	0	6	43
Fat necrosis	2	14	6	43
Skin contracture	0	0	13	93
Entire flap contracture†	0	0	3	21

* All except one patient received reconstruction with transverse rectus abdominis muscle flap (TRAM).

† Entire flap contracture would need an additional flap to create the breast mound.

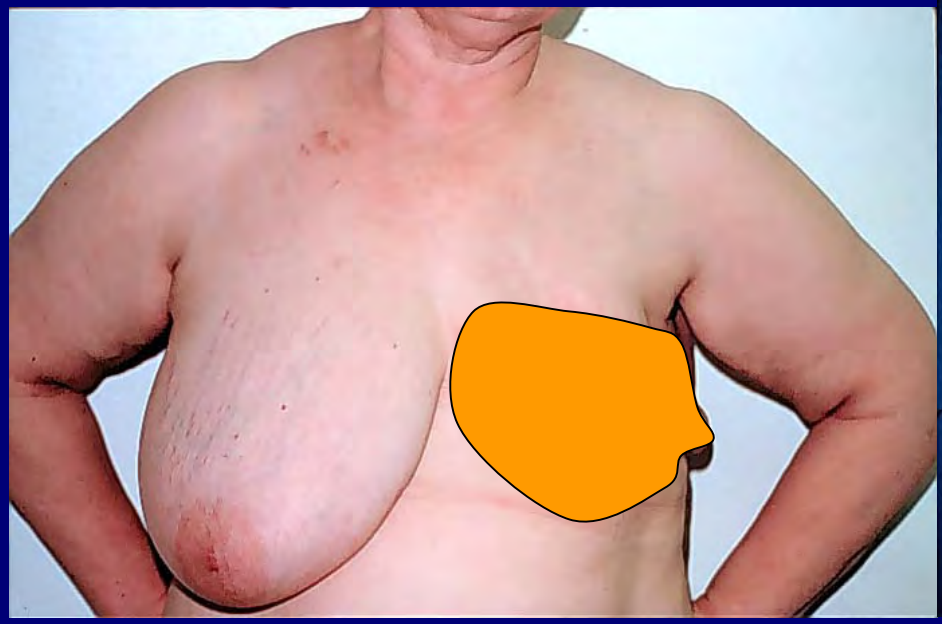
Tran NV. et. al. *Plastic & Reconstructive Surgery.* 106(2):313-7; 2000.

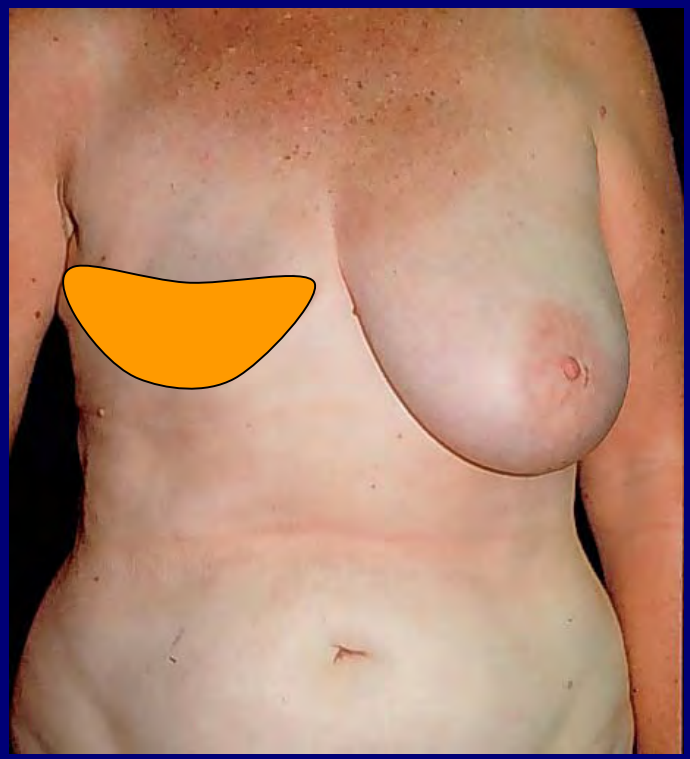
Radiotherapy and Reconstruction

Oct. 2000

64 Gy
Jan. 2001

Jan. 2002





Radiotherapy and Reconstruction

Timing

- Immediate
- Delayed
- “Delayed Immediate”

Overview

- Background
  - Reconstruction and multidisciplinary care
  - Techniques
- Preoperative therapies
  - Chemotherapy
  - Radiotherapy
  - Recurrent disease
- Research opportunities

Research Opportunities

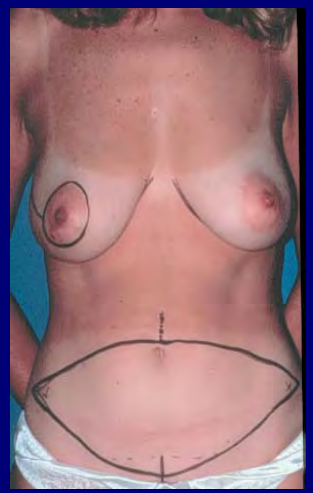
1. Characterize deformity-related morbidity.
   - Focused Quality of Life studies

Pre-operative

Post-operative

Implant reconstruction

Latissimus Dorsi flap +
Implant reconstruction



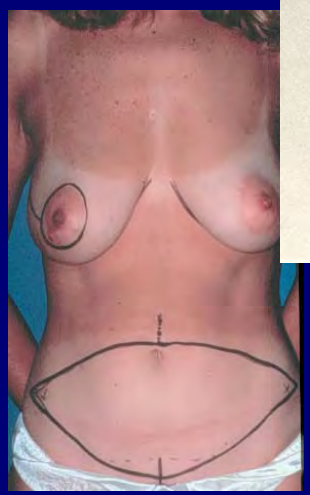
Autologous tissue
reconstruction

Pre-operative

Post-operative

Implant reconstruction

us Dorsi flap +
econstruction



ous tissue
reconstruction

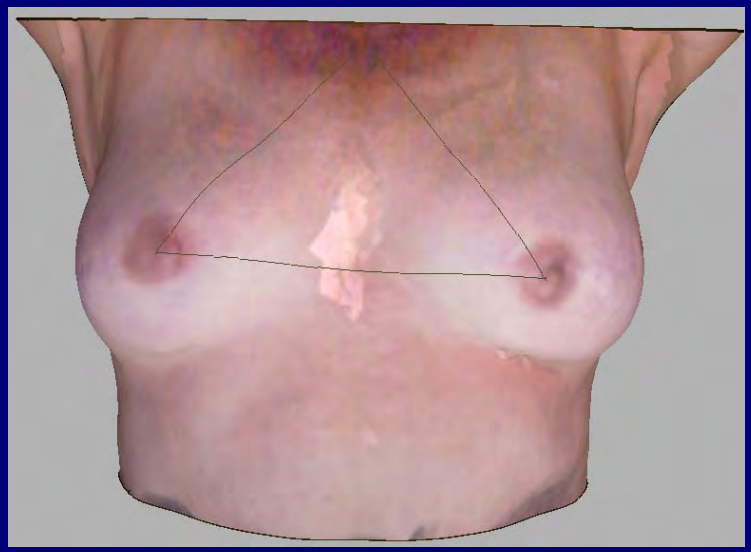
Quality of Life

- Results equivocal
- Selection bias
  - Patients generally successful self-selecting treatment options.
- Patients of interest are on the margins.

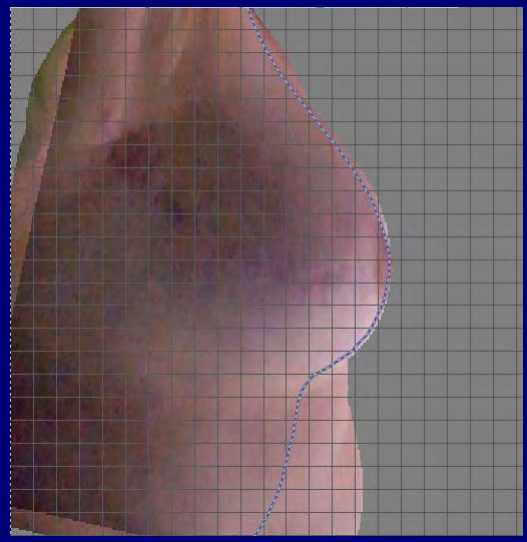
Research Opportunities

1. Characterize deformity-related morbidity.
   - Focused Quality of Life studies
   - Quantitative outcomes
     - Objective assessment of deformity
     - Individualized assessment of morbidity

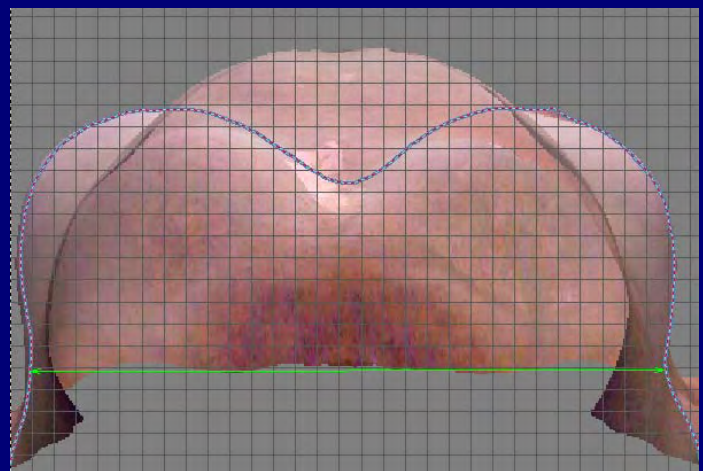
Breast Shape Analysis



Conventional anthropomorphic measurements



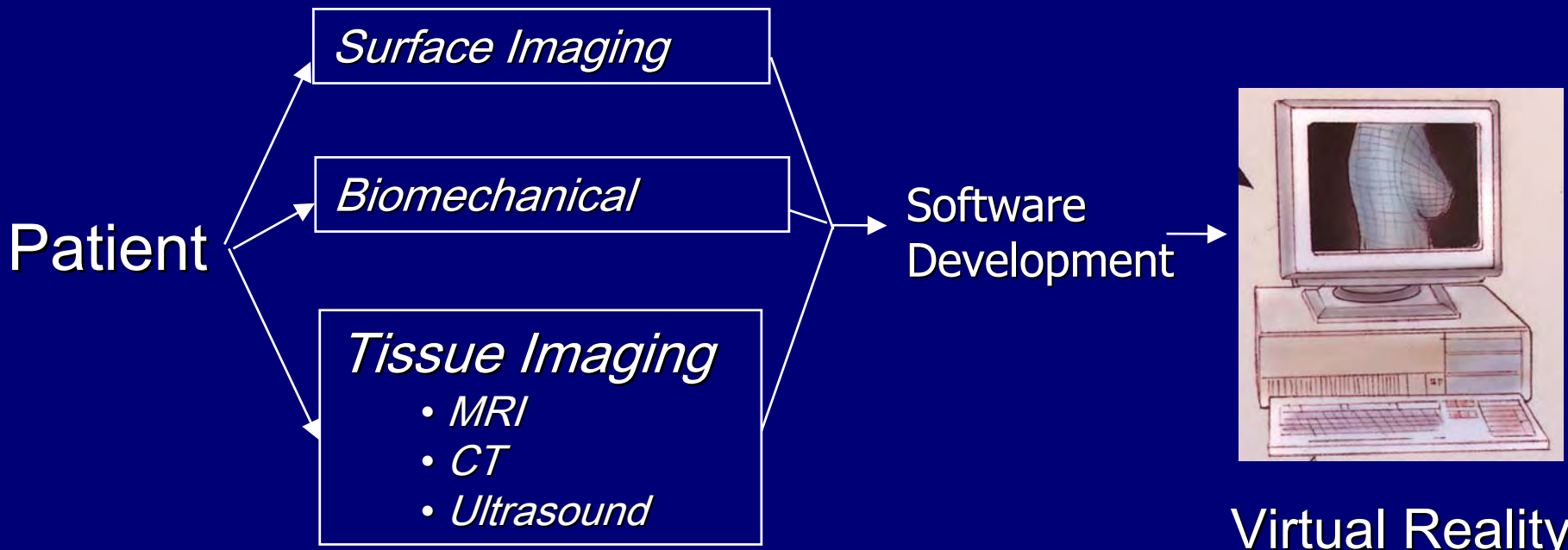
Contours and cross sections



Research Opportunities

1. Characterize deformity-related morbidity.
   - Focused Quality of Life studies
   - Quantitative outcomes
     - Objective assessment of deformity
     - Individualized assessment of morbidity
   - Patient specific, predictive

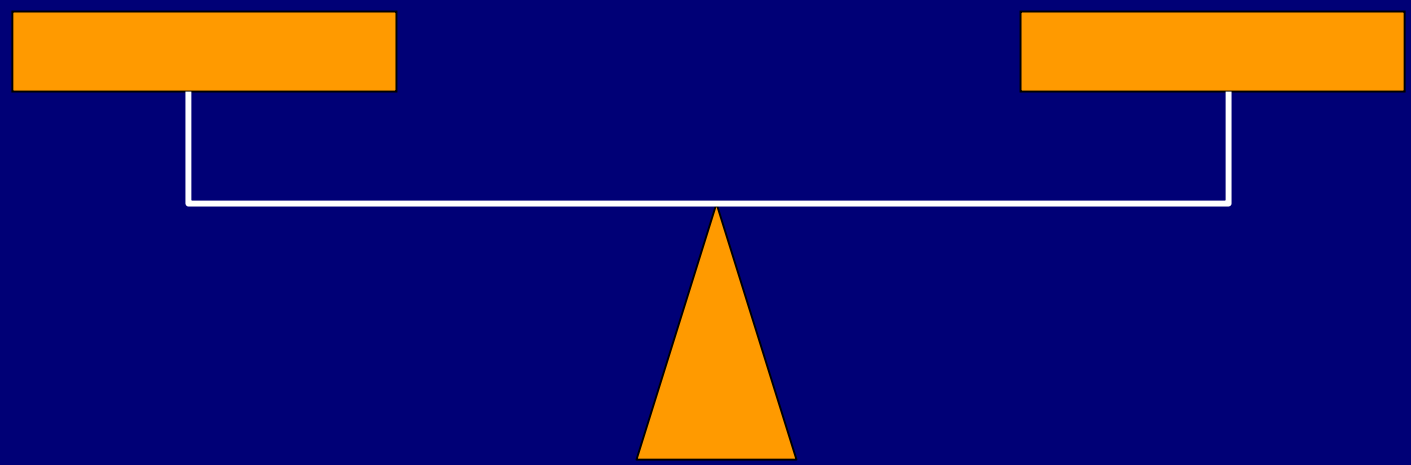
Digital Breast Simulation



Therapeutic Risk/Benefit

Undesirable outcomes

Cancer-free Survival
+
Freedom from Suffering



Patient Treatment Options

Short-term Opportunities

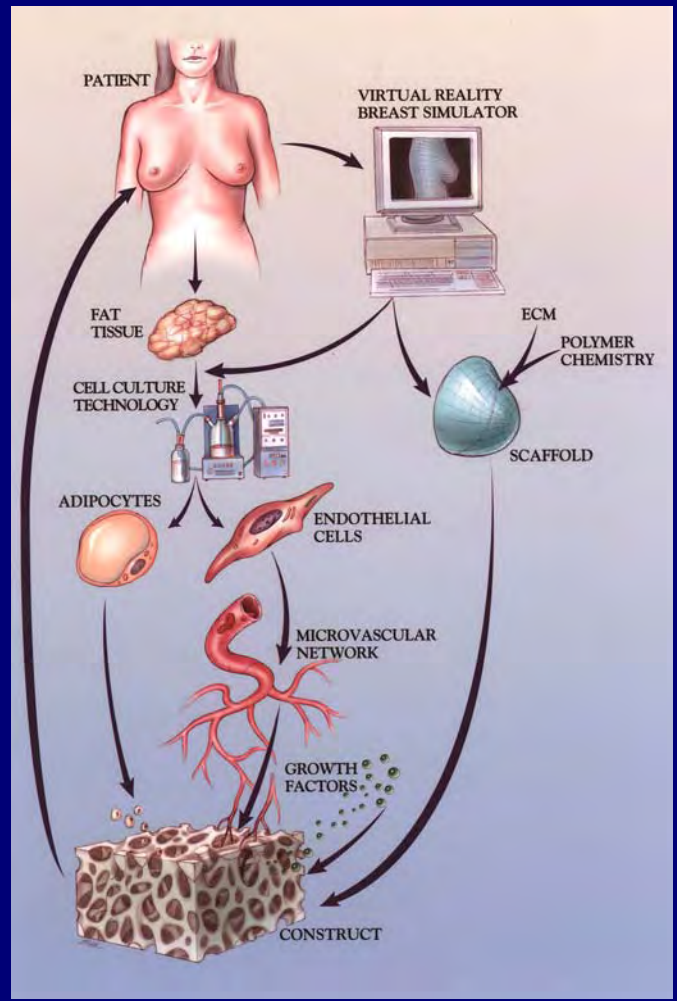
1. Characterize deformity-related morbidity.
   - Focused Quality of Life studies
   - Quantitative outcomes
     - Objective assessment of deformity
     - Individualized assessment of morbidity
   - Patient specific, predictive

2. Educational and decision-making aids

Research in these areas translates immediately into benefits for 100% of patients!

Long-term Opportunities

- Regenerative medicine
- Tissue Engineering



Thank you