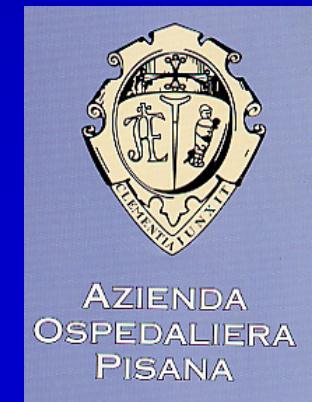


Novità nella riparazione tessutale

Marco Romanelli

Sezione di Riparazione Tessutale Cutanea
Clinica Dermatologica
Università di Pisa



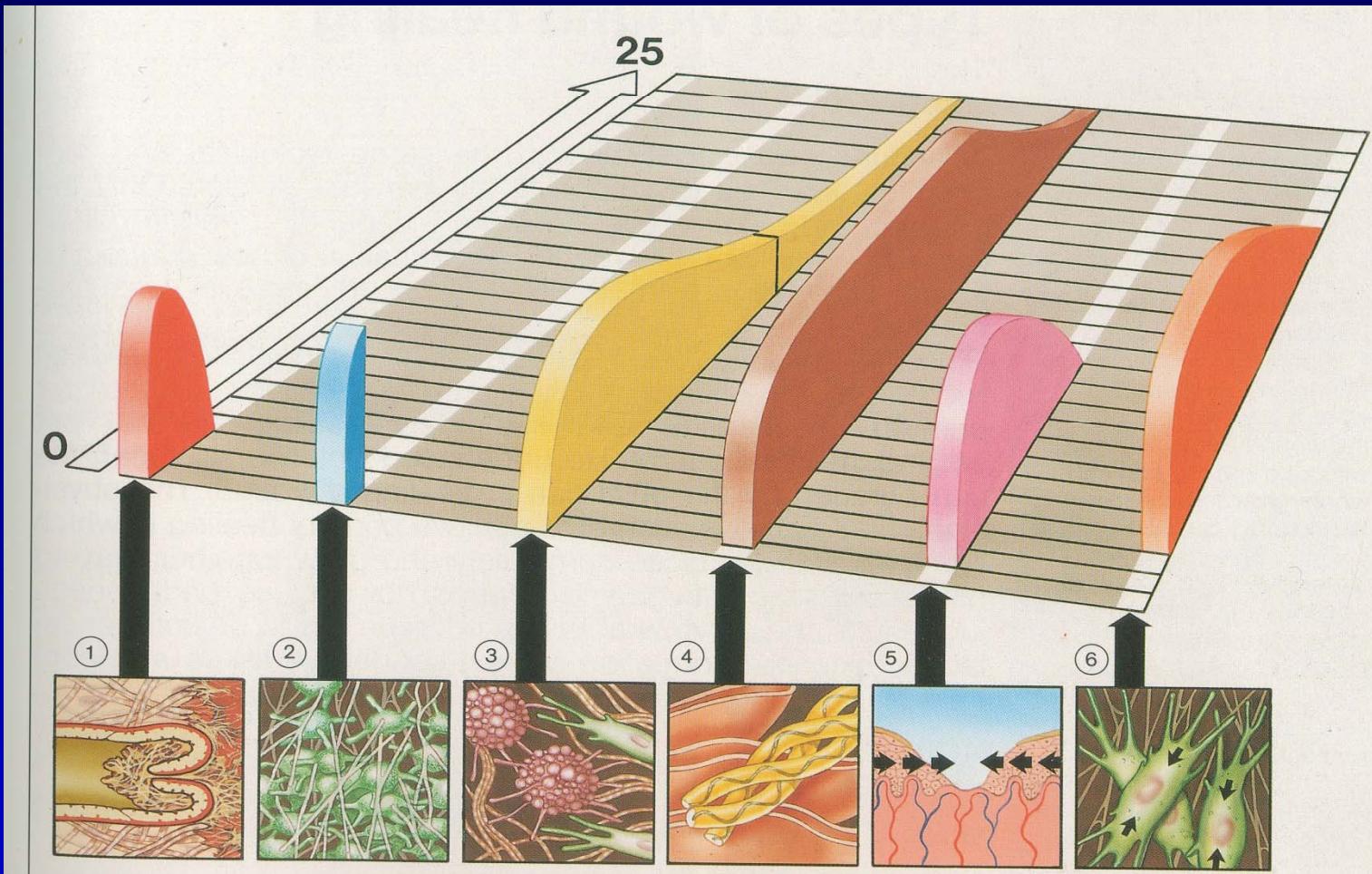


Figure 21 Time relationship between the different wound healing processes:

- | | |
|-----------------------|-----------------------------|
| 1 = vascular response | 4 = formation of new tissue |
| 2 = blood coagulation | 5 = epithelialisation |
| 3 = inflammation | 6 = contraction |

Riparazione Tessutale Cutanea

Lesioni acute e croniche



Acuto Vs Cronico

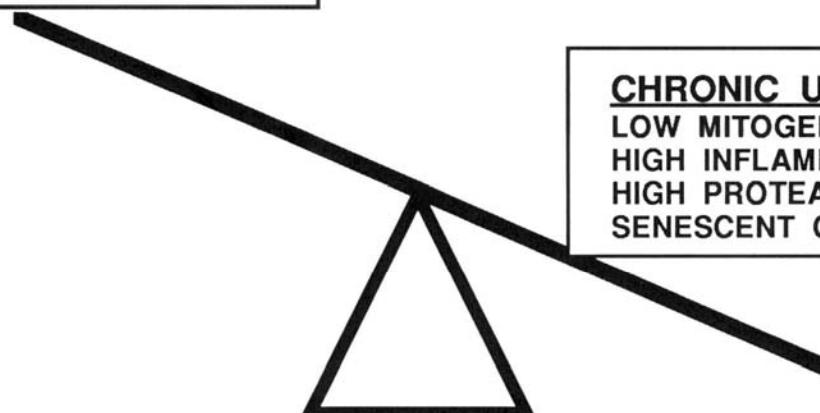
MOLECULAR ENVIRONMENT OF WOUNDS

HEALING WOUNDS

HIGH MITOGENIC ACTITITY
LOW INFLAMMATORY CYTOKINES
LOW PROTEASES
MITOTICALLY COMPETENT CELLS

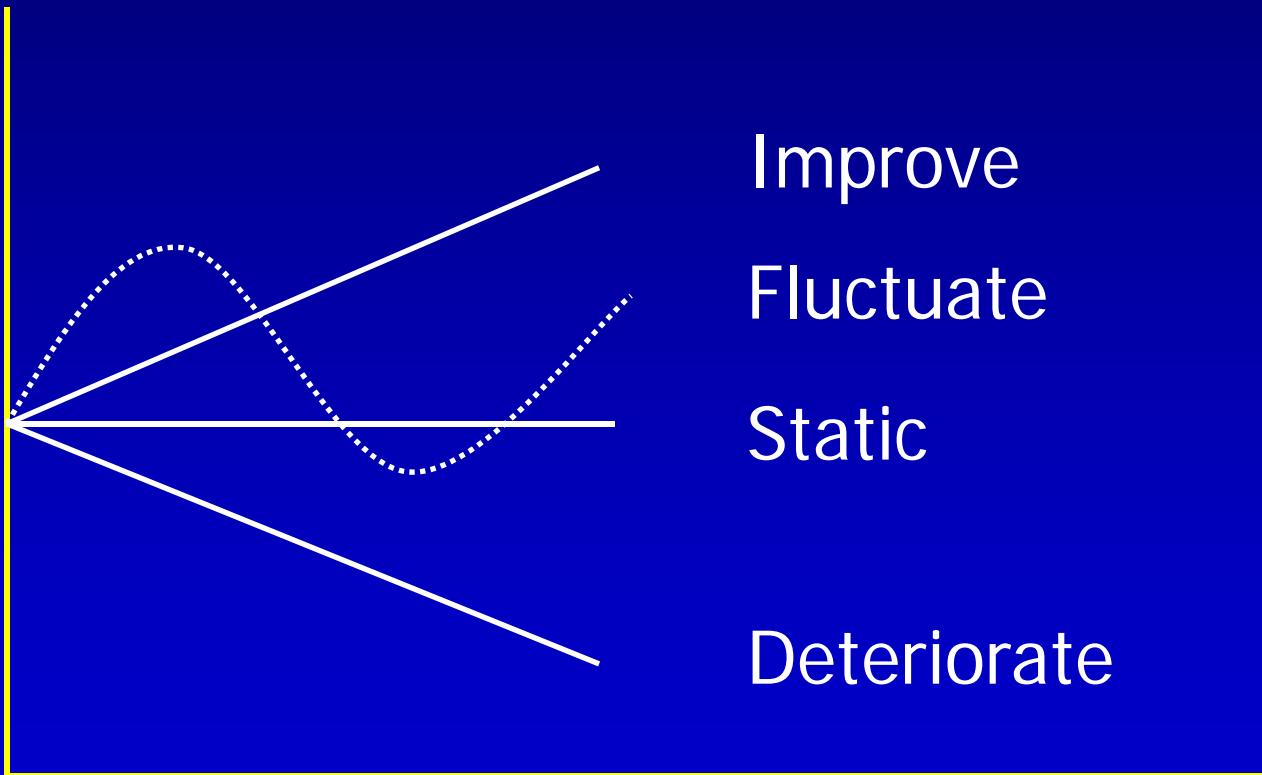
CHRONIC ULCERS

LOW MITOGENIC ACTITITY
HIGH INFLAMMATORY CYTOKINES
HIGH PROTEASES
SENESCENT CELLS



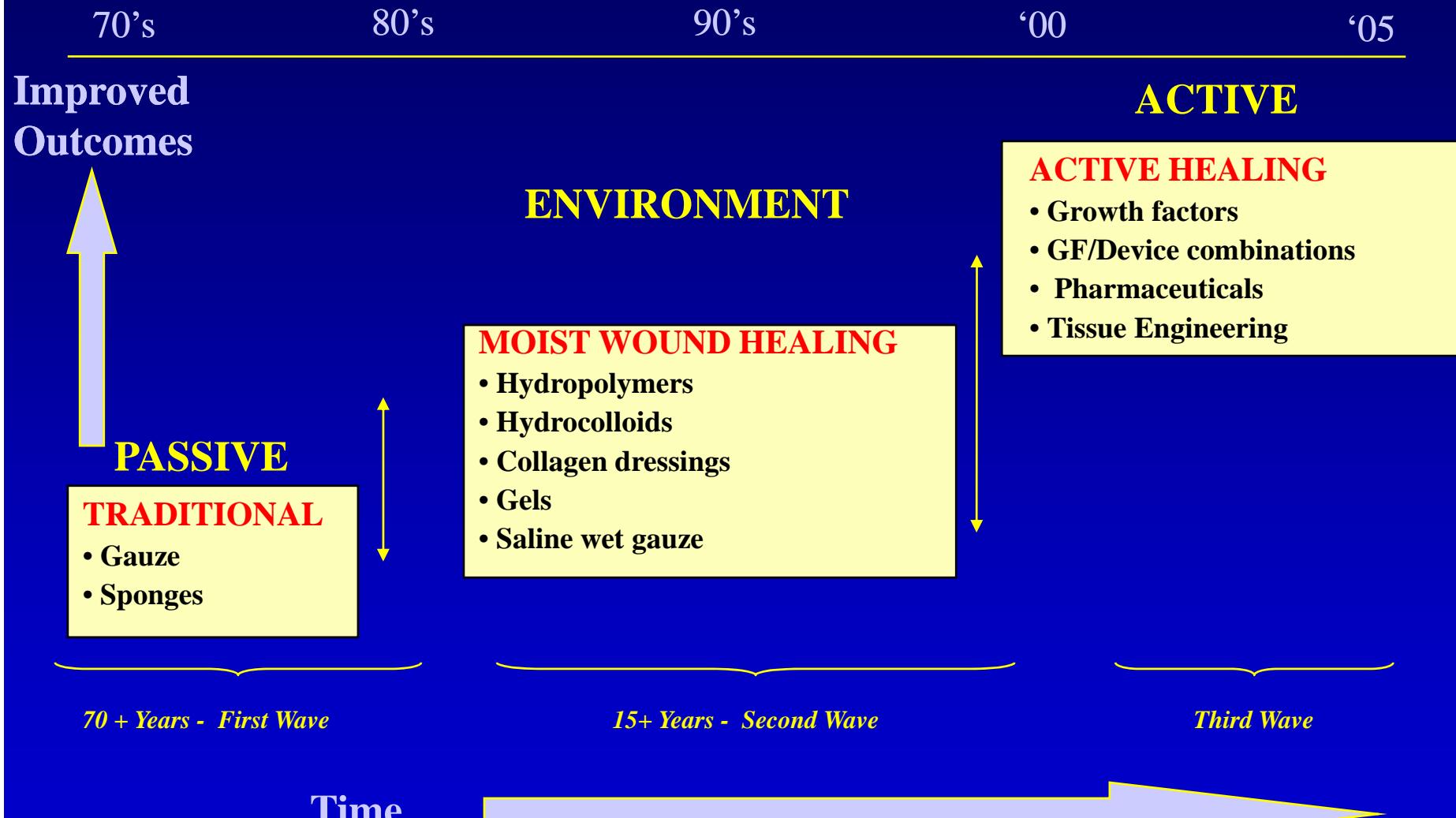
Chronic wound healing

Clinical Evidence



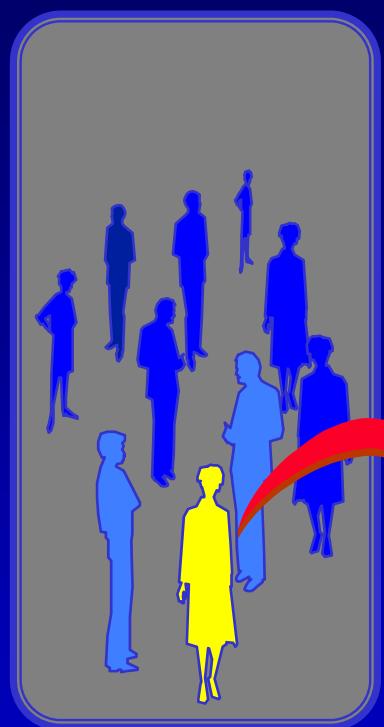
K. Harding 2004

The Wound Healing Market is Becoming Increasingly Technology Driven

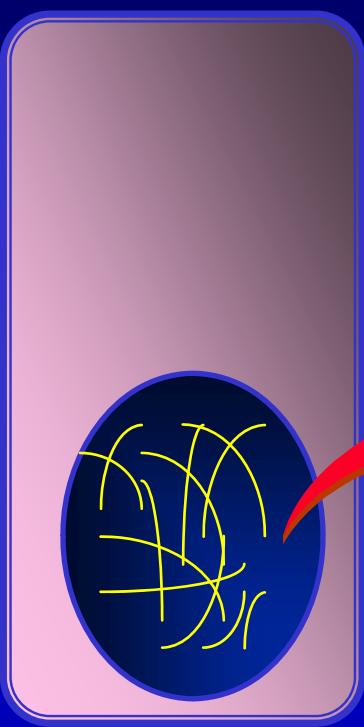




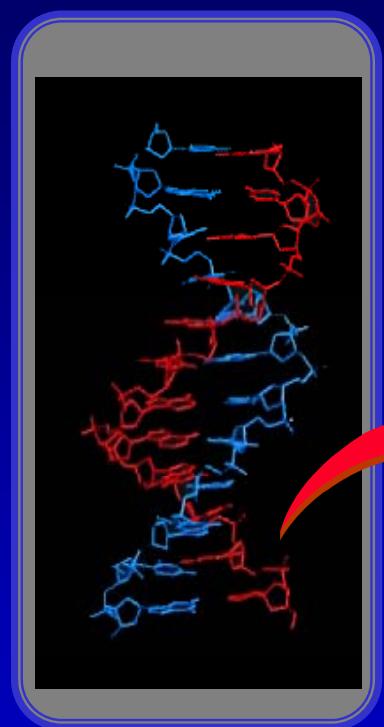
Wound Care:
ambulatoriale
o
ospedalizzazione



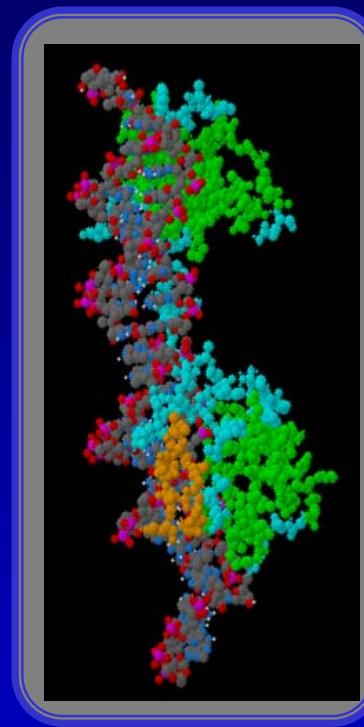
HUMAN



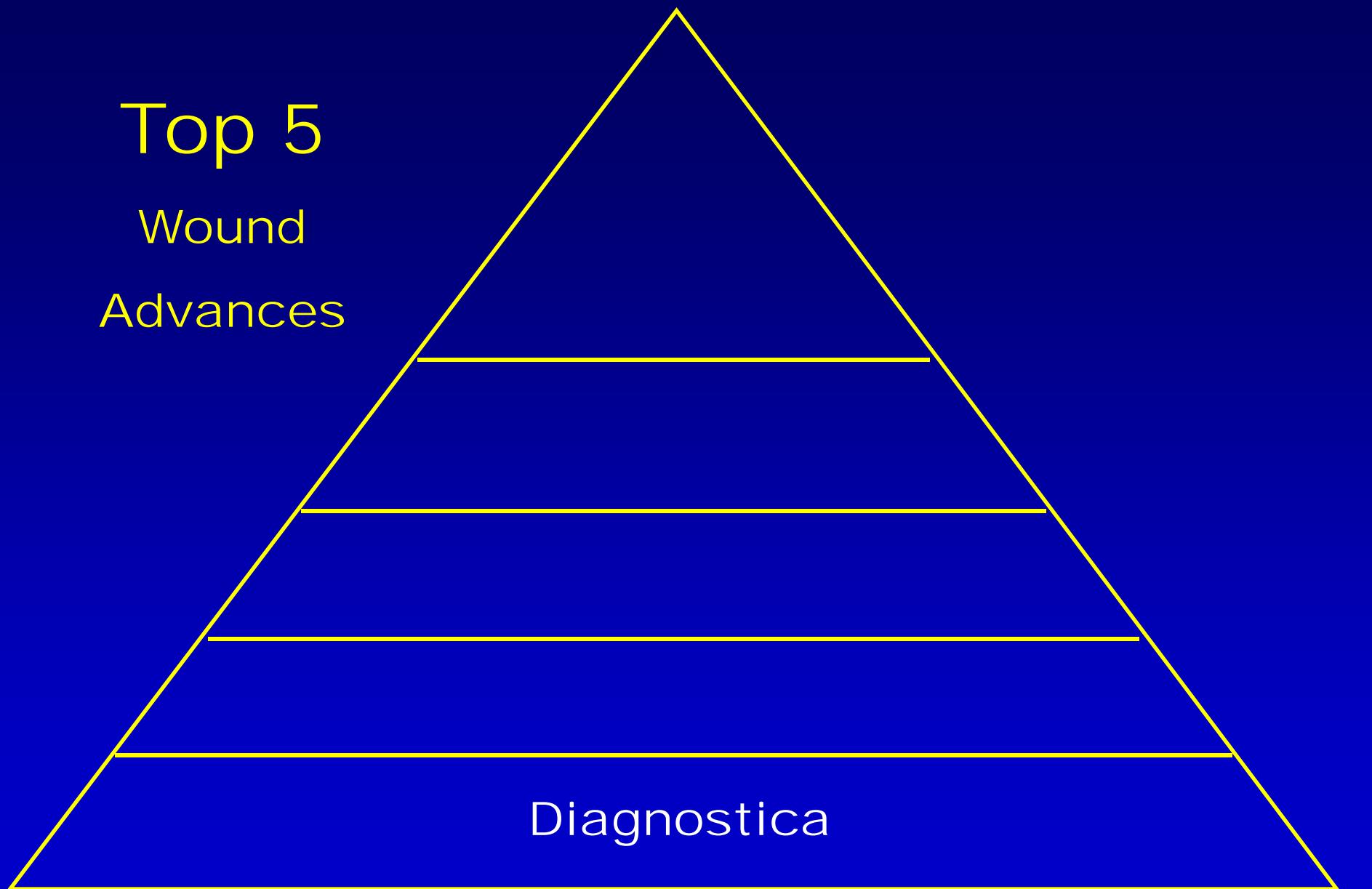
CELL



GENE



PROTEIN



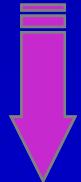
Top 5
Wound
Advances

Diagnostica

Wound Management

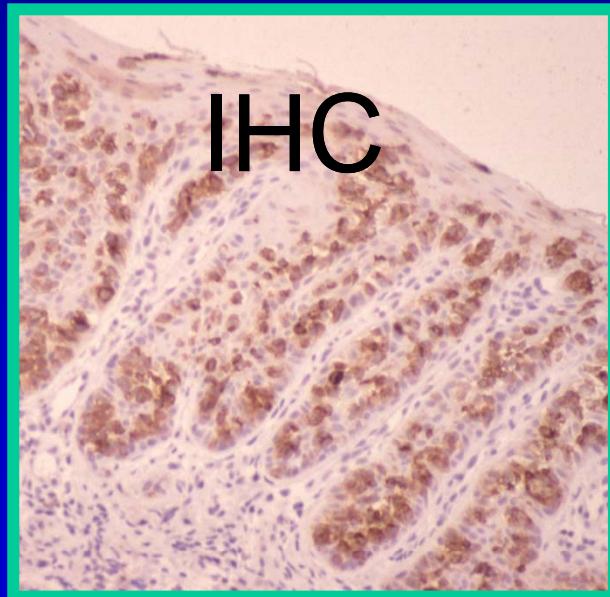
Valutazione morfologica

- Adeguata 90%
- Incompleta 10%

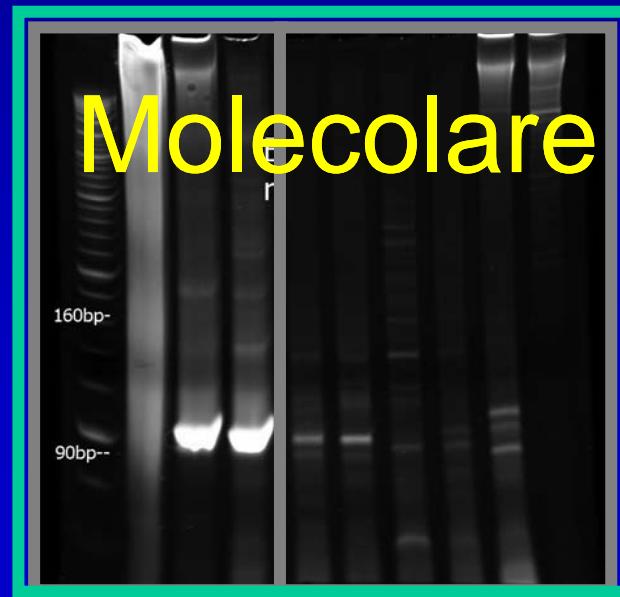


Ancillary Tests

Valutazione paziente

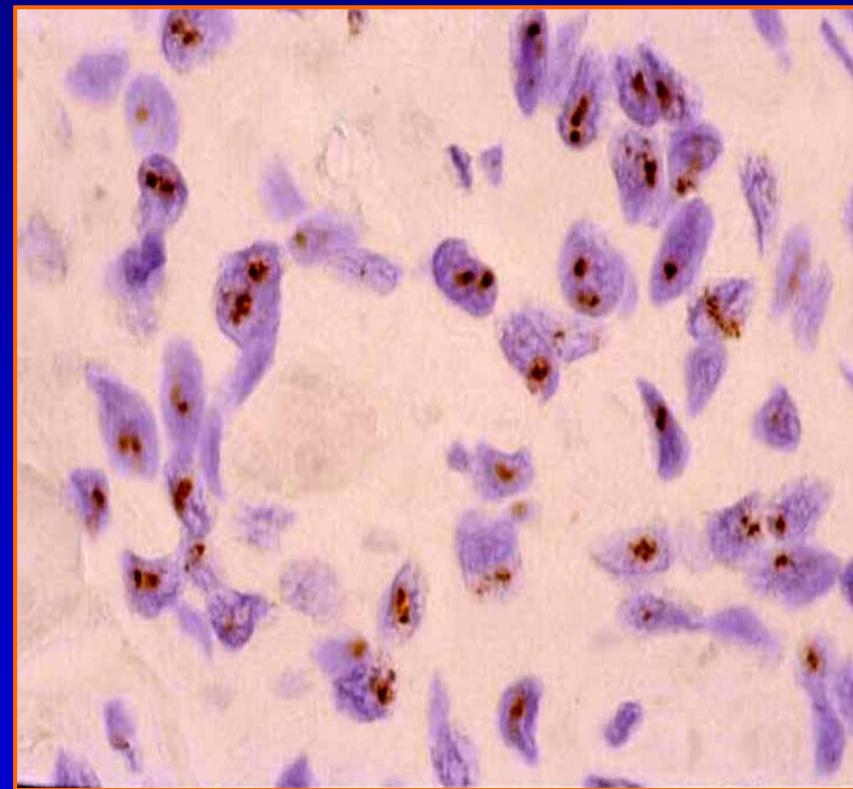
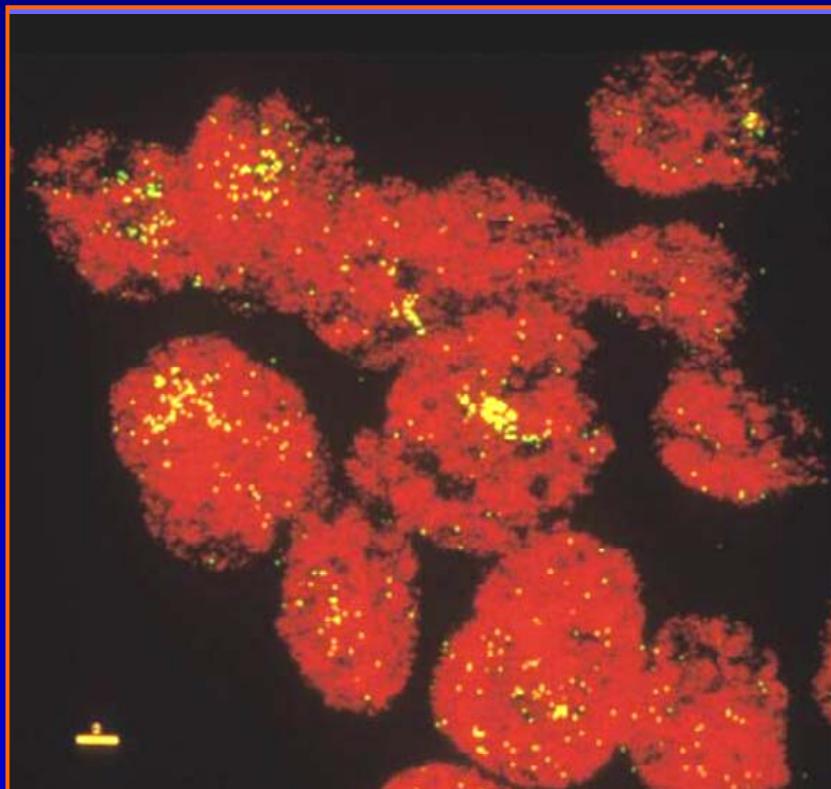


IHC



Molecolare

In Situ Hybridization



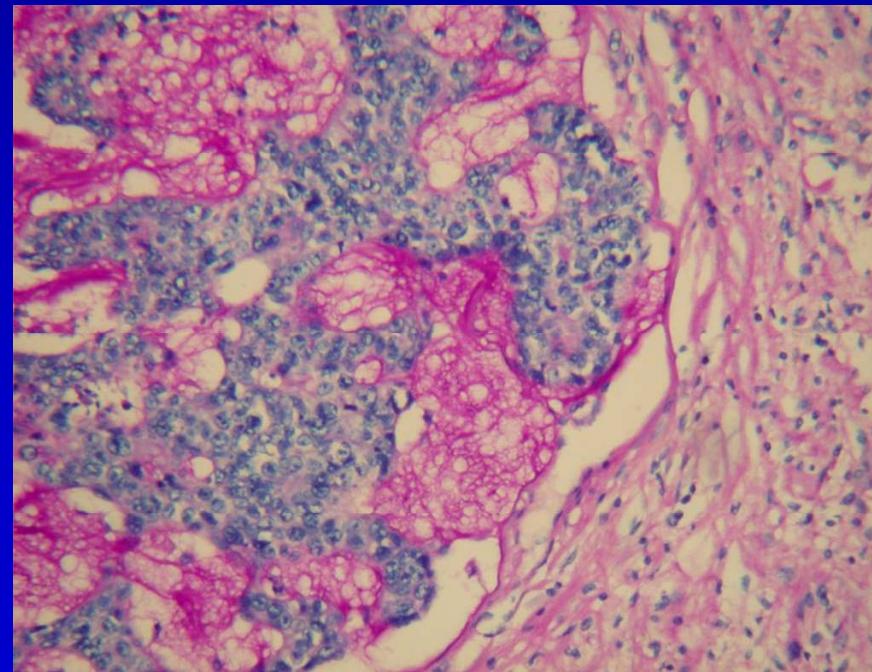
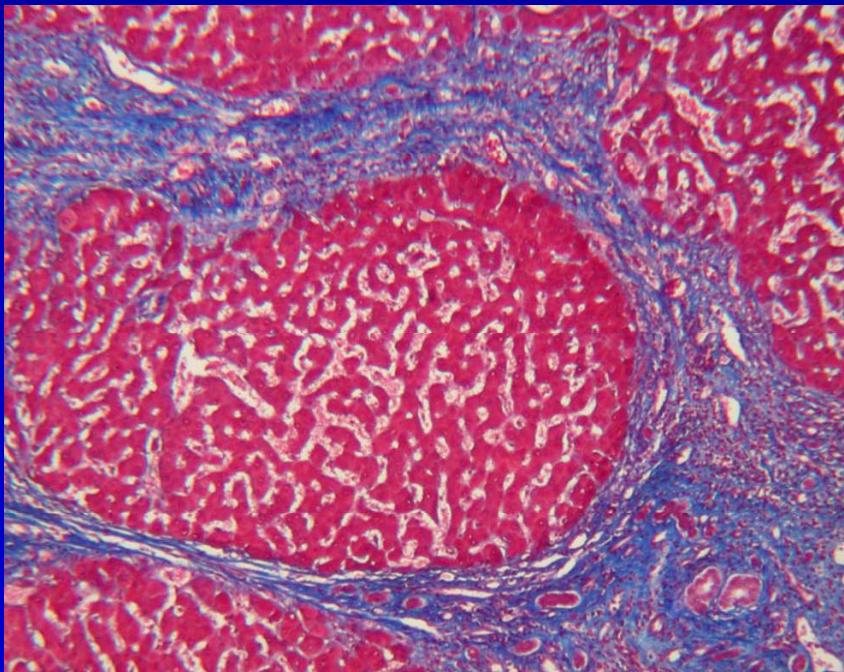
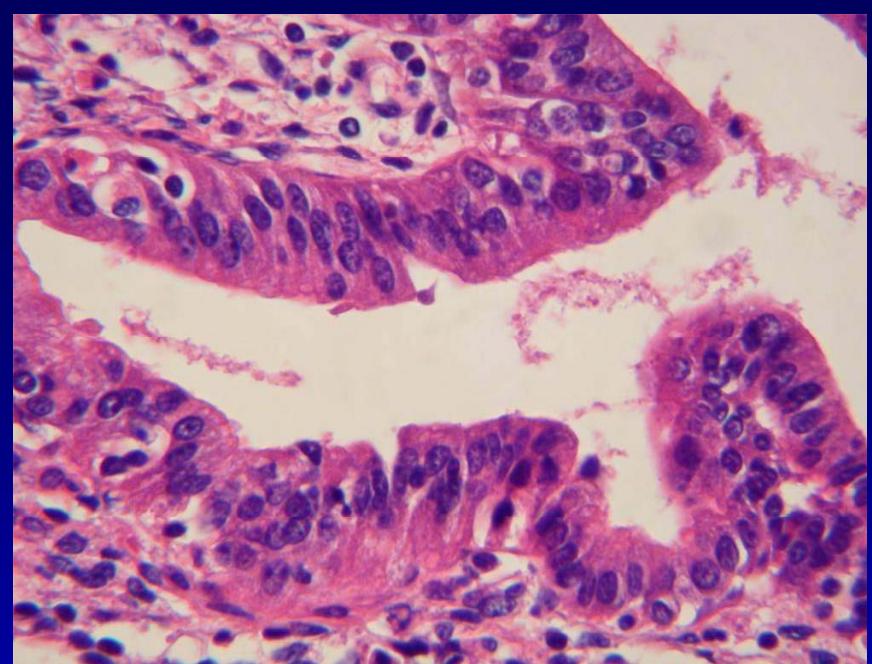
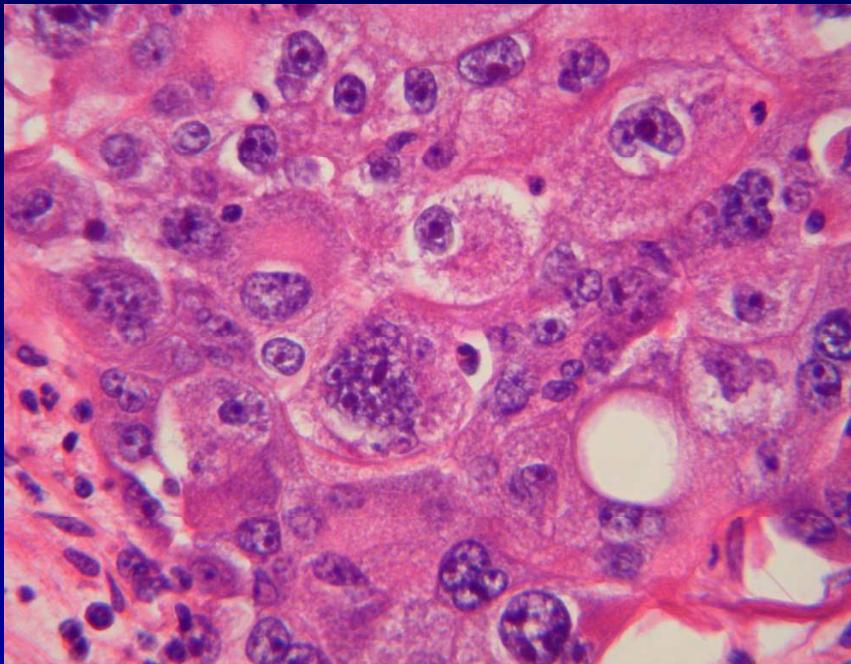
Anatomic Pathology / MICROWAVE-ASSISTED RAPID TISSUE PROCESSING

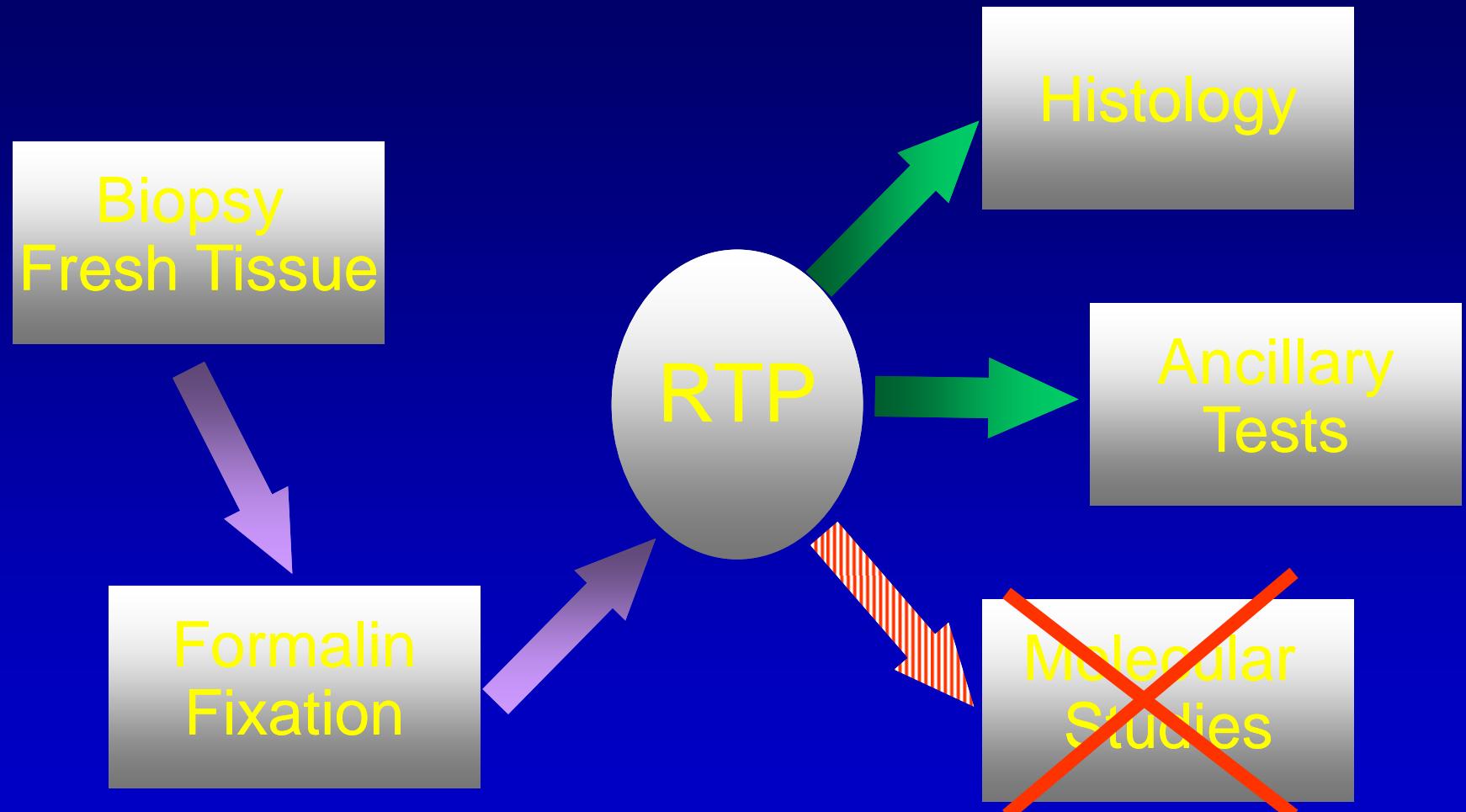
Experience With an Automated Microwave-Assisted Rapid Tissue Processing Method

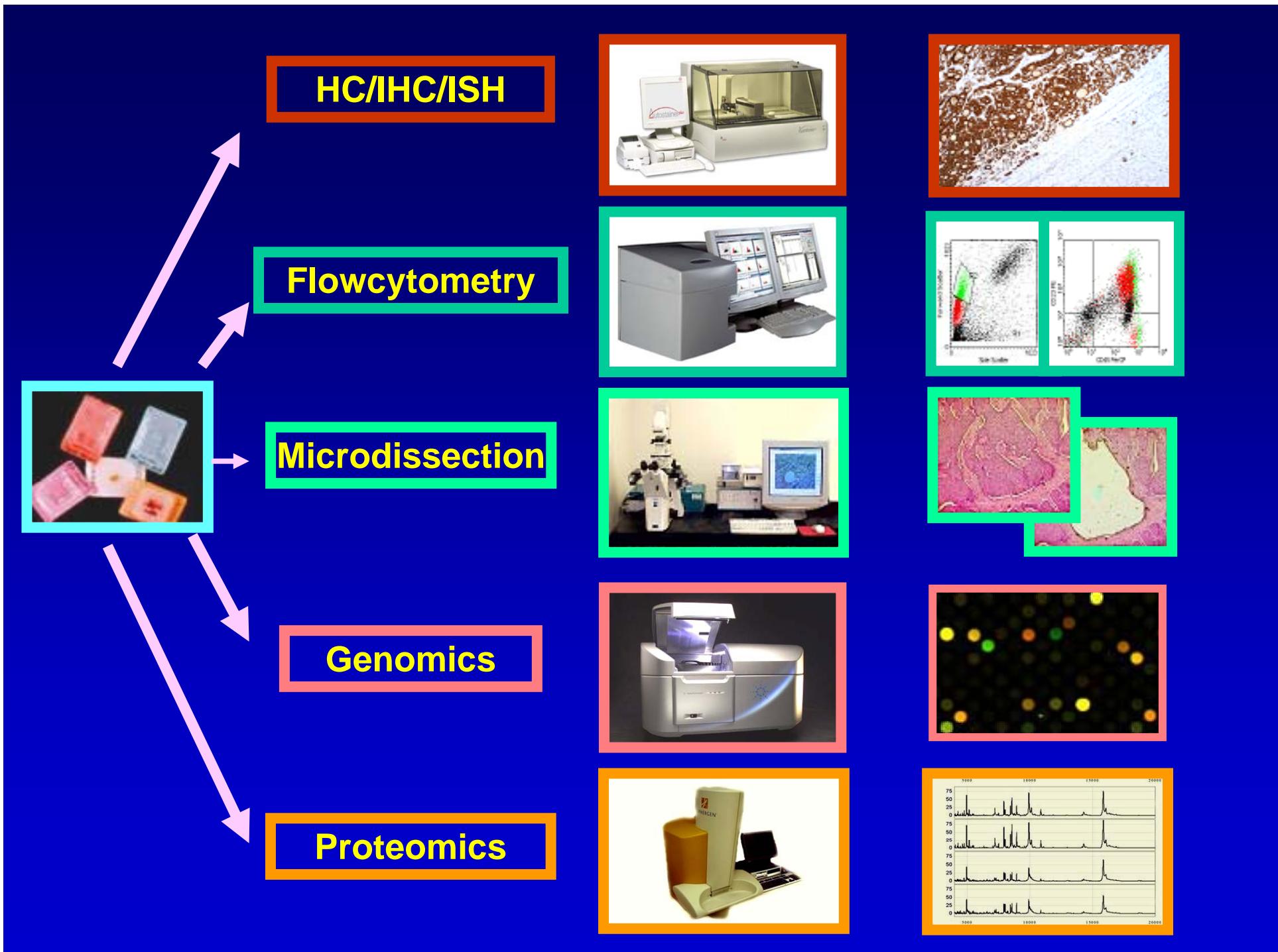
Validation of Histologic Quality and Impact on the Timeliness
of Diagnostic Surgical Pathology

Azorides R. Morales, MD, Mehdi Nassiri, MD, Rima Kanhoush, MD, Vladimir Vincek, MD, PhD,
and Mehrdad Nadji, MD

Am J Clin Pathol 2004; 121: 528-536

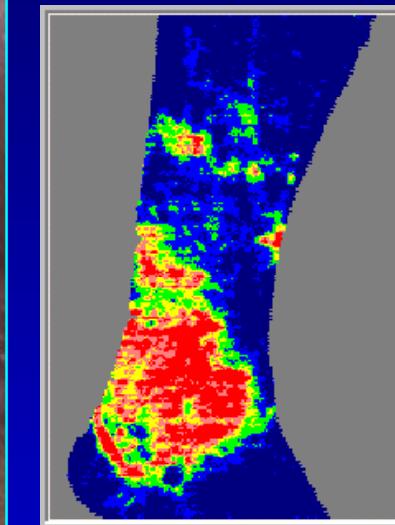






Tissue-Based “omics”

Impatto sulla diagnosi e
gestione delle malattie





SilhouetteMobile in
clinical use

Medical Silhouette

Solution for wound imaging,
measurement and documentation

- Measures area, depth, volume
- Allows structure entry of wound assessment notes
- Efficient
- Repeatable
- Portable
- Easy to use
- Non-contact
- Data accessible over the web
- Integrates with Health Information Systems

ARANZ Medical SilhouetteMobile



Off-the-shelf PDA (personal computing device)

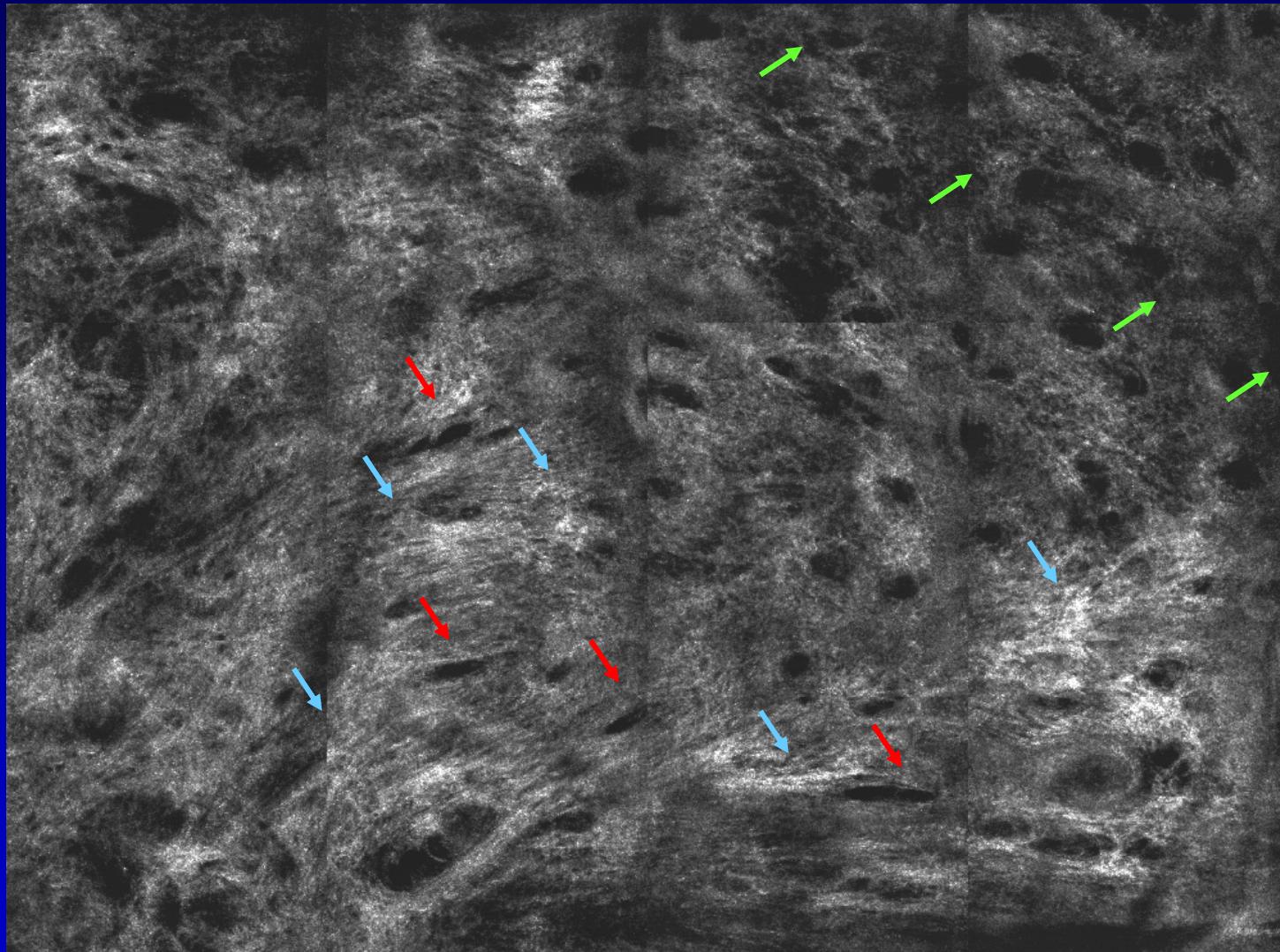
Silhouette application software for:
- image capture,
- analysis (area, depth & volume)
- report generation
- email / fax / backup

VivaScope® 3000 Confocal Microscope

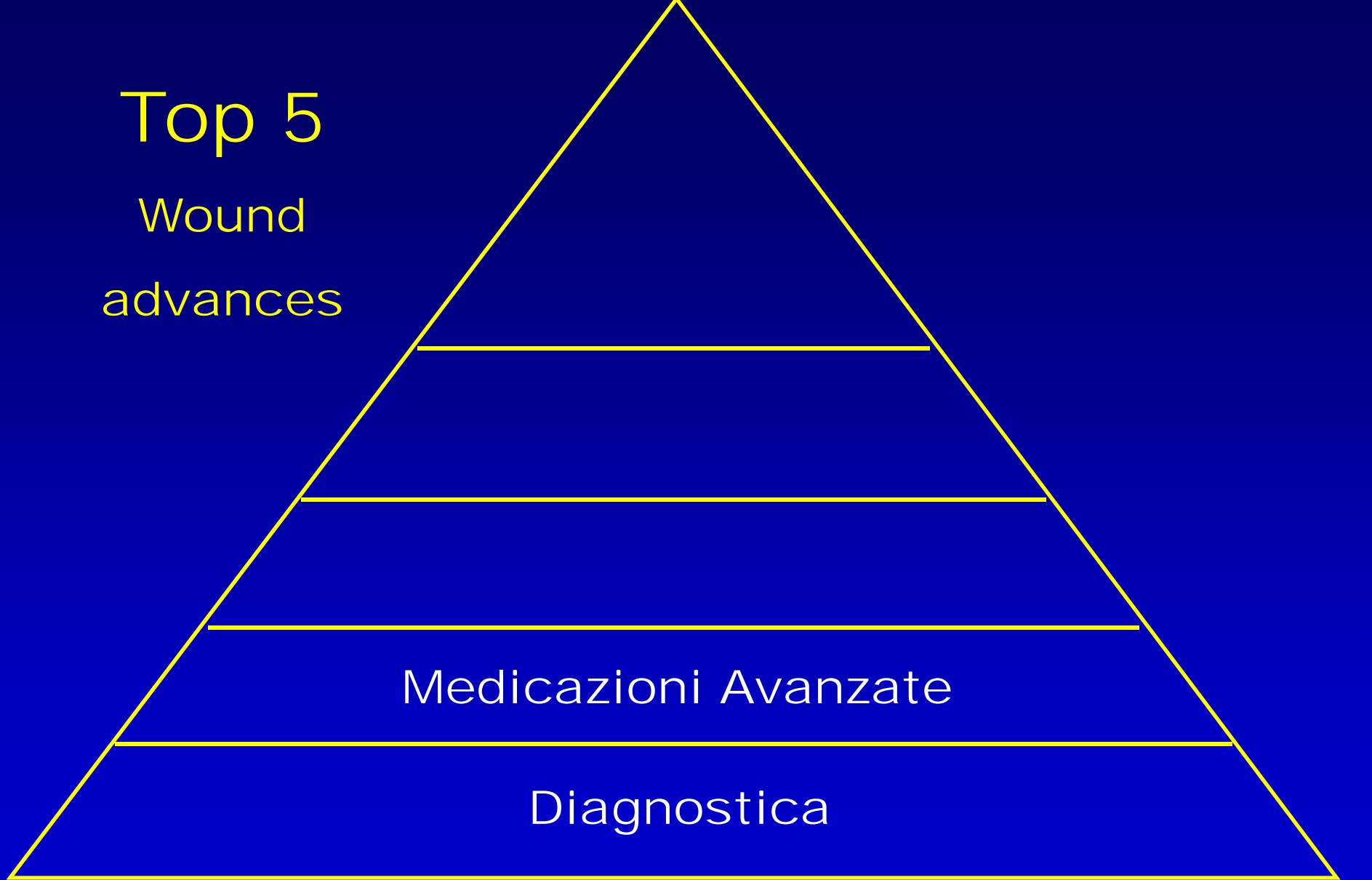


The VivaScope® 3000 is a hand-held laser confocal microscope capable of video-rate imaging of living tissue at the cellular level. This device potentially can be used as an *in vivo* or intra-operative device to examine the morphological features and dynamic processes of tissue in real time. The non-invasive “optical biopsy” generated by the VivaScope provides medical practitioners with information that can be used as an adjunct to histology.

- Provides real time, video rate sample assessment
- Images cells *in vivo* for diagnostic and therapeutic research
- Allows for observation of a site over time to study progression of disease
- Assists in pre-operative and intra-operative margin evaluation



Composite map or VivaBlock measuring 2 x 1.5 mm taken at the top of the reticular dermis shows dense scar tissue (blue arrows) and elongated capillaries (red arrows) adjacent to a normal papillary dermis (green arrows).



Top 5
Wound
advances

Medicazioni Avanzate
Diagnostica

Medicazioni Avanzate



Terapia delle infezioni

Opzioni

- Debridement o farmaci
- Antisettici o antibiotici
- Topici o sistemici
- Breve o lunga durata
- Prevenzione o trattamento
- Tradizionale o nuova

Terapia delle infezioni

Tradizionale

Miele

- Cooper 1999

Yoghurt

-

Acido acetico

-

Potassio Permanganato

-

Larve

- Church, Thomas

Terapia delle infezioni

Avanzata

VAC®

- Argenta, Banwell

Citochine

- Edmonds

Normotermia

- Melling 2002

MMP inhibitori

- Cullen, Veves

Ulcera da pressione grado III con infezione superficiale



Dopo terapia con argento nanocristallino





basale



dopo 3 settimane

**ulcera
ischemica**



Medicazione a base di Collagene Equino





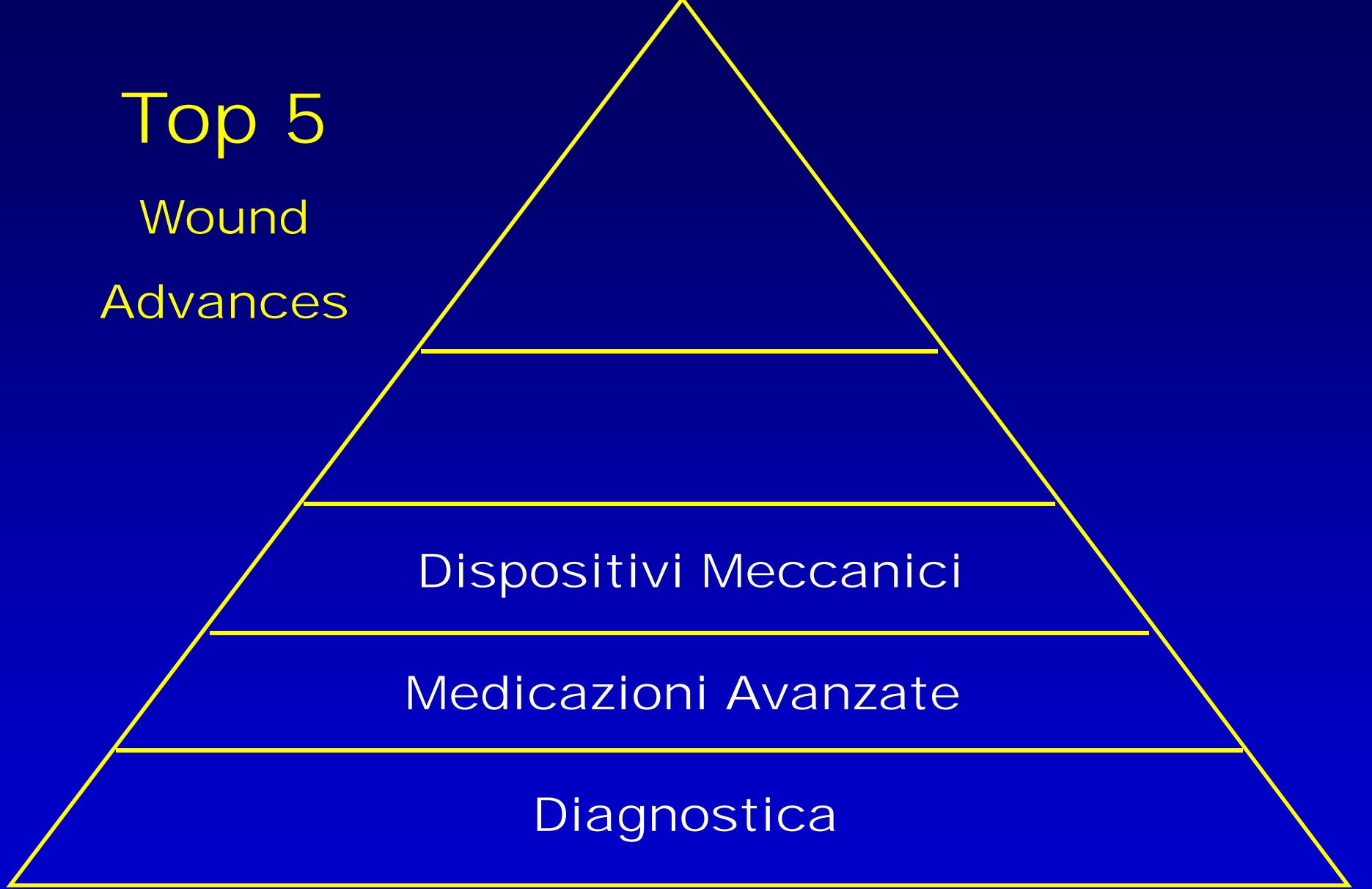


basale



dopo 32 giorni

Top 5 Wound Advances



Dispositivi Meccanici

Medicazioni Avanzate

Diagnostica

V.A.C.® system



Indicazioni

- **Ulcere croniche**
 - Ulcere diabetiche
 - Ulcere da pressione
 - Ulcere venose
- **Ferite acute e traumatiche**
 - Ferite subacute
- **Deiscenze chirurgiche**
- **Innesti a rete**
- **Lembi di rotzione**

Carica batterica

Superficie

Profondità

Terapia Fotodinamica (PDT) in wound healing



Killing of cutaneous microbial species by photodynamic therapy

Zeina B. et al. Br J Dermatol 2001; 144: 274-278

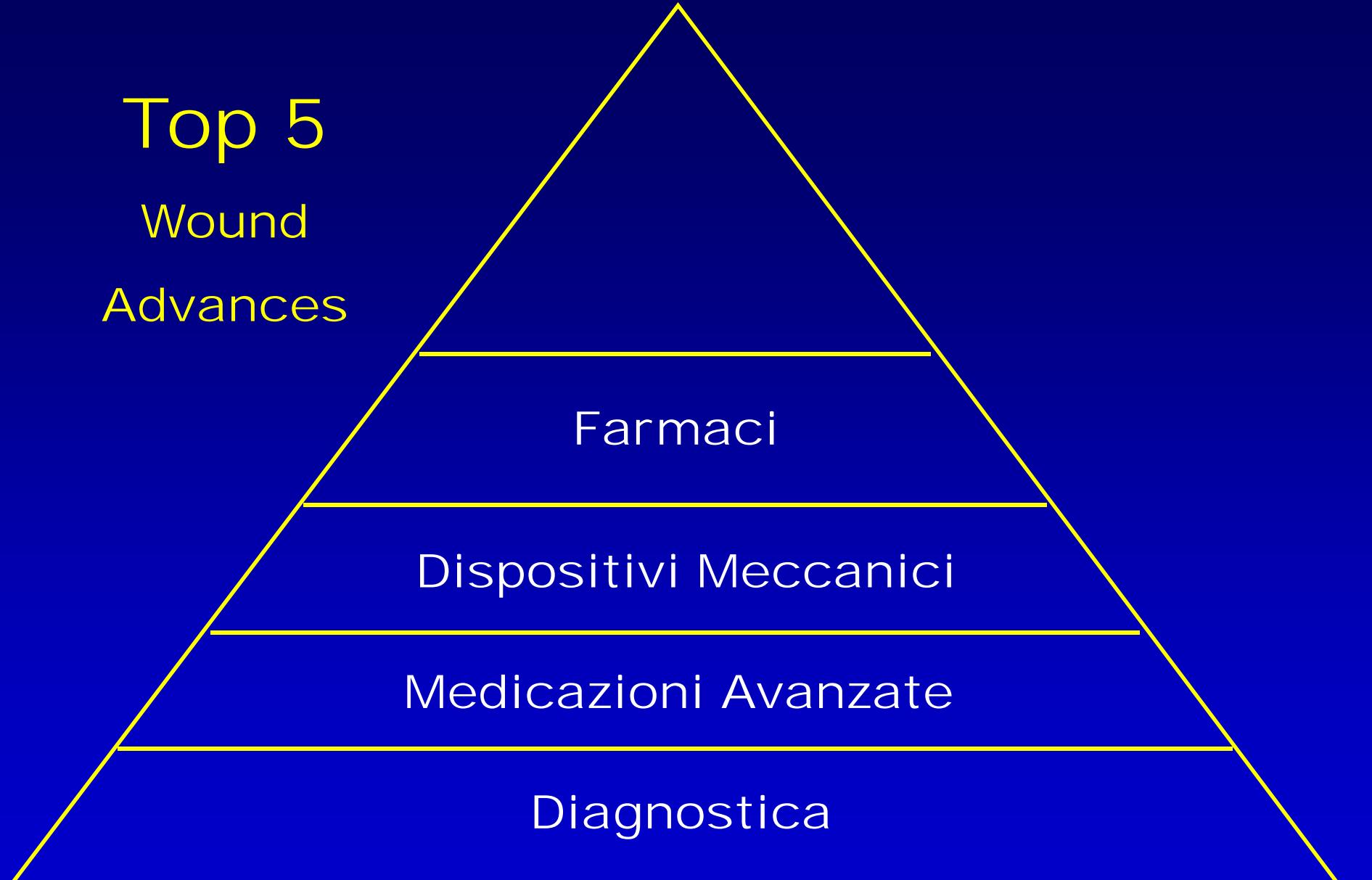
Cytotoxic effects of antimicrobial photodynamic therapy on keratinocytes
in vitro

Zeina B. et al. Br J Dermatol 2002; 146: 568-573

**Prolonged skin allograft survival after
photodynamic therapy (PDT)
associated with modification of donor
skin antigenicity**

Modestus O.K. et al
Transplantation 1997; 63: 810 -
817

Top 5 Wound Advances



Pyoderma Gangrenosum

Geren S. et al WOUNDS 2003; 15: 49-53

**Infliximab 4-6 mg/kg
Weeks 0, 2, and 8 then every 6-8 weeks**

Top 5 Wound Advances

Staminali
Ingegneria
Tessutale

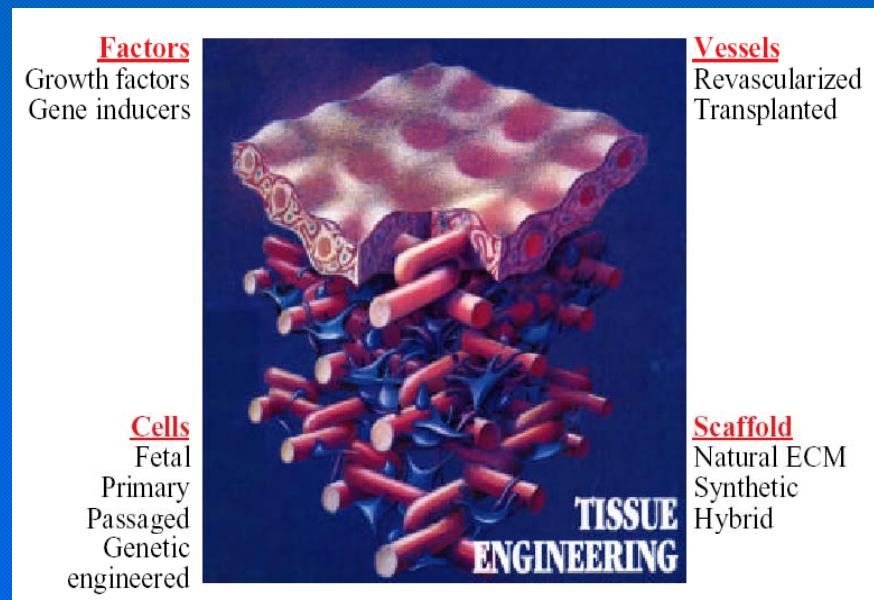
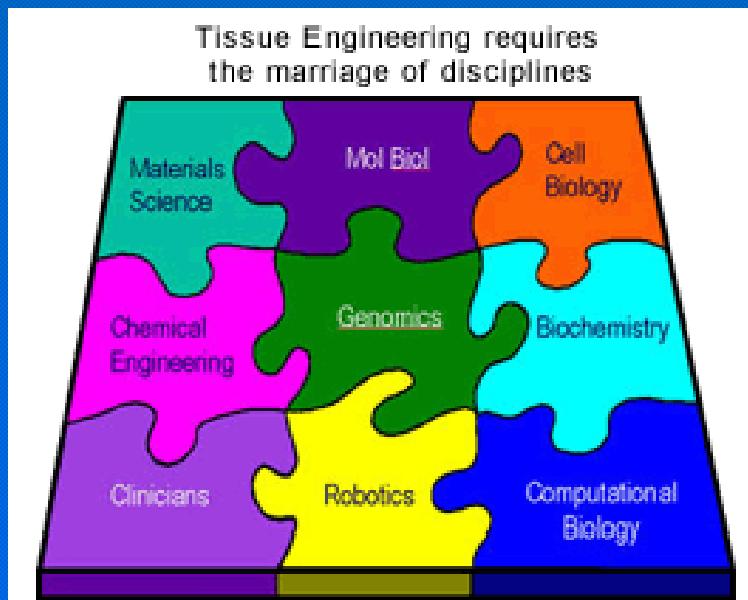
Farmaci

Dispositivi Meccanici

Medicazioni Avanzate

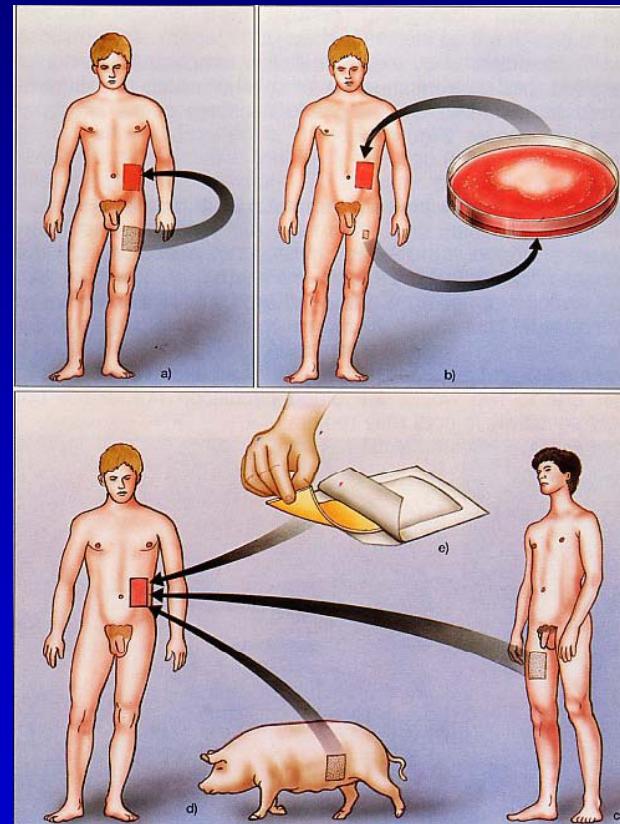
Diagnostica

Tissue Engineering

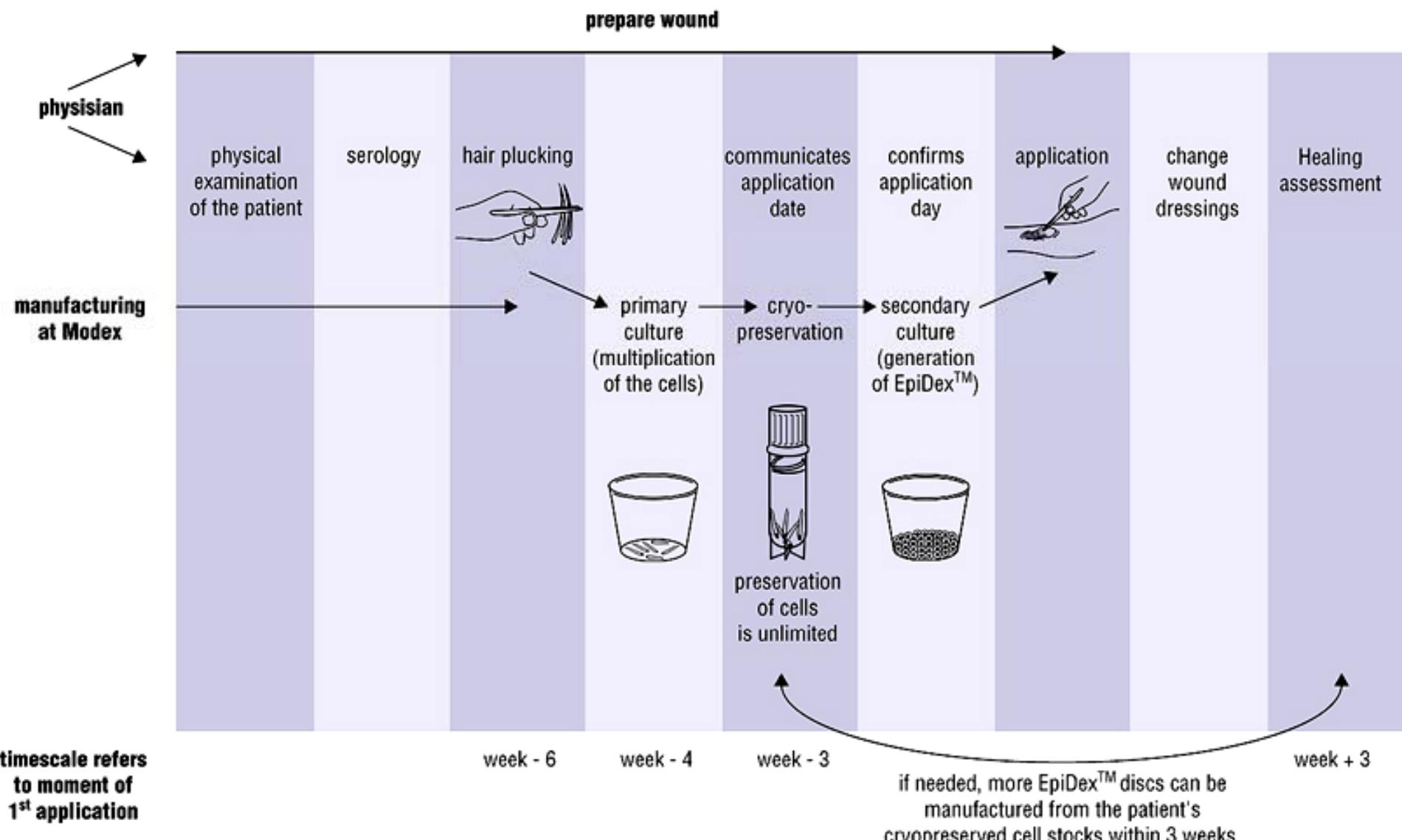


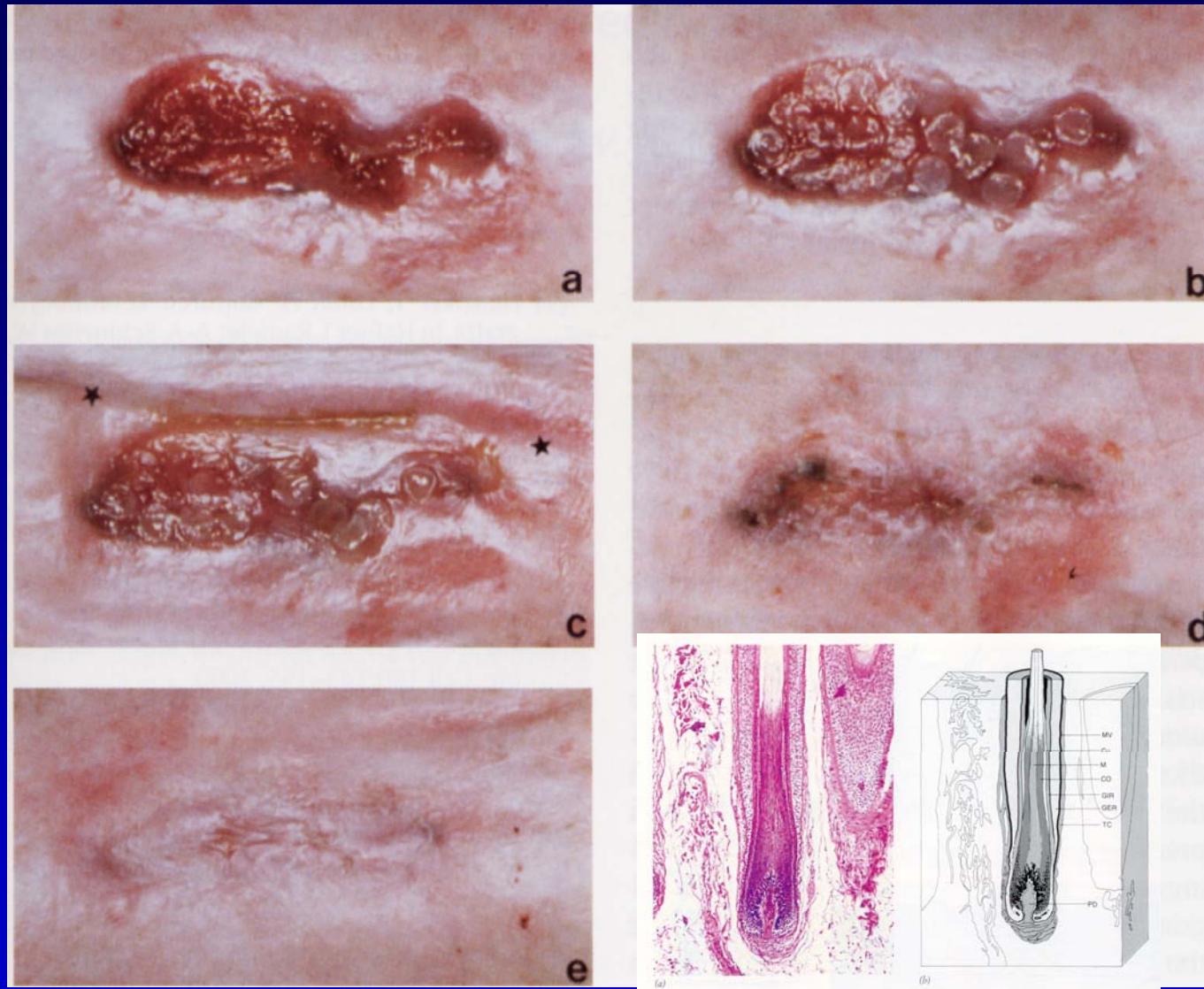
Skin grafting and tissue engineering

- Dermagraft®
- Apligraf®
- Integra®
- Transcyte®
- Epicel®
- TissueTech®
- AlloDerm®
- Biobrane®

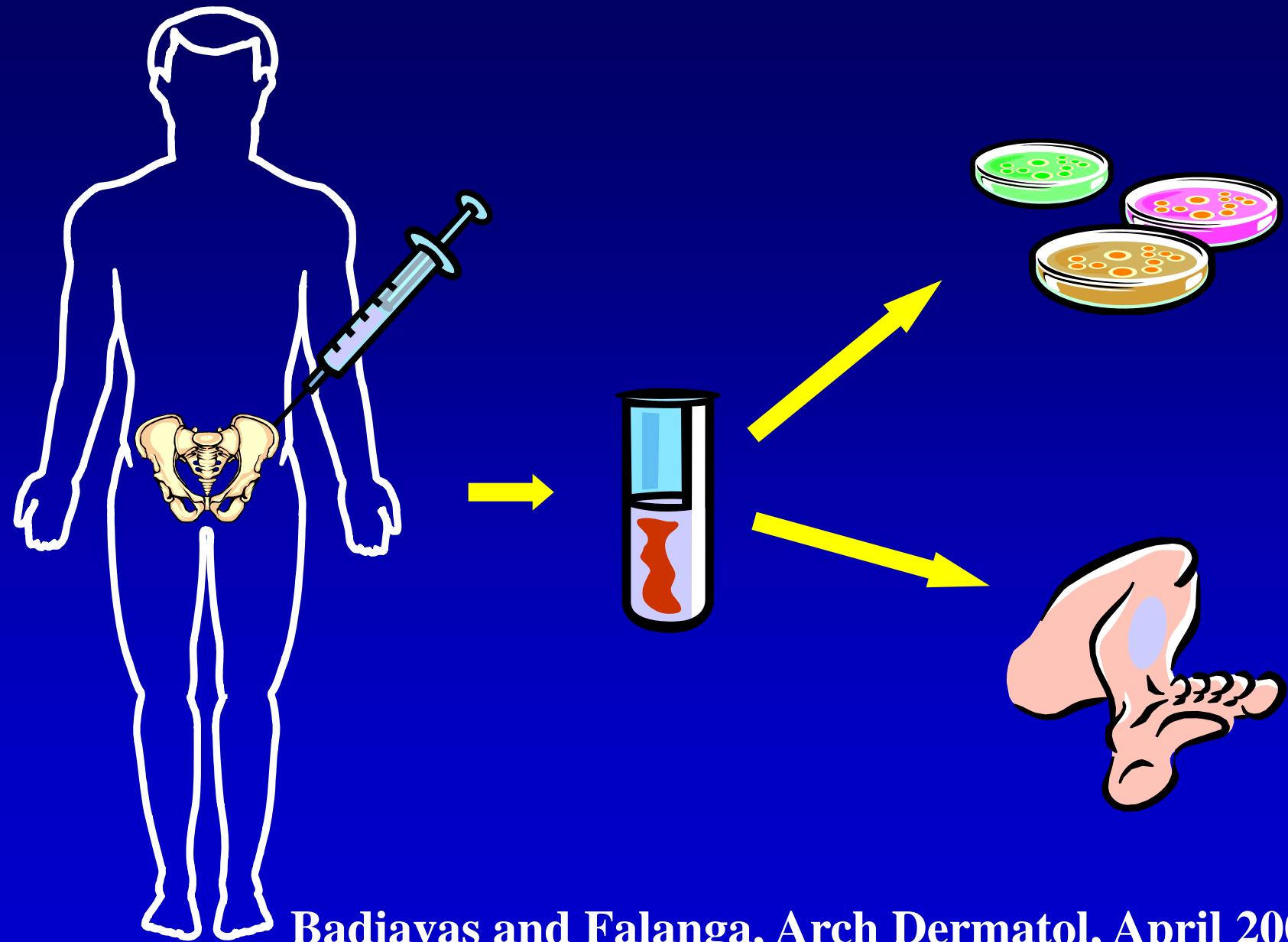


Tissue engineering from hair





Epidermal equivalents from autologous outer root sheath cells for chronic wounds
T. Hunziker et al.
J. Invest Dermatol 1996;107:128-135



Badiavas and Falanga, Arch Dermatol, April 2003

Use of autologous bone marrow-derived cells to treat chronic wounds.

Arch Dermatol, April 2003



Fattori di crescita come agenti terapeutici

- Vantaggi

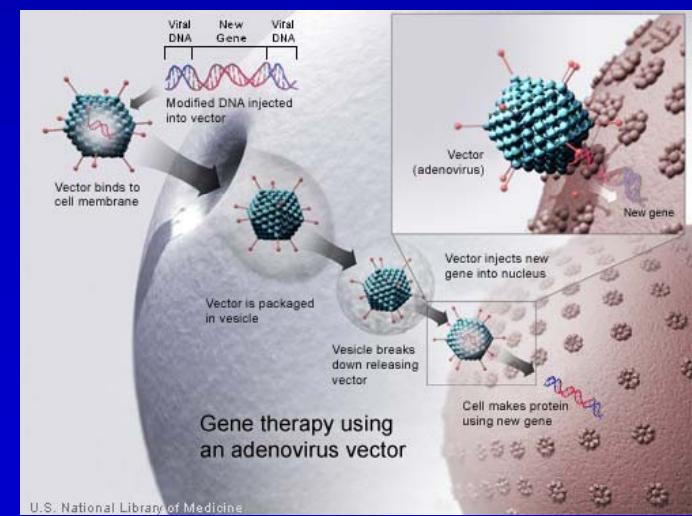
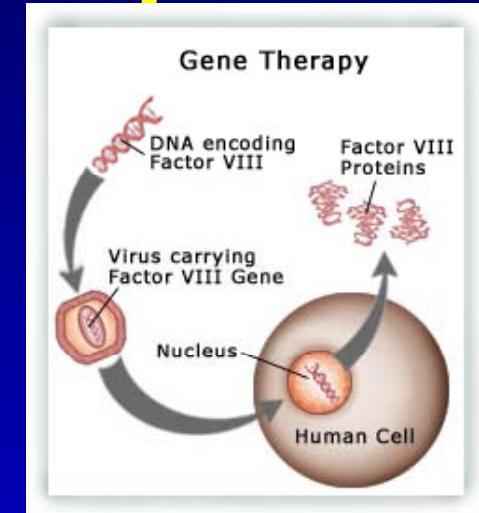
- Azione locale
- Effetto selettivo
- Componenti naturali processo rip. tessutale
- Bassa tossicità

- Svantaggi

- Costi produzione (ricombinanti) proteine
- Effetti sistemici ad alte dosi
- Durata
- Biodisponibilità
- Somministrazione

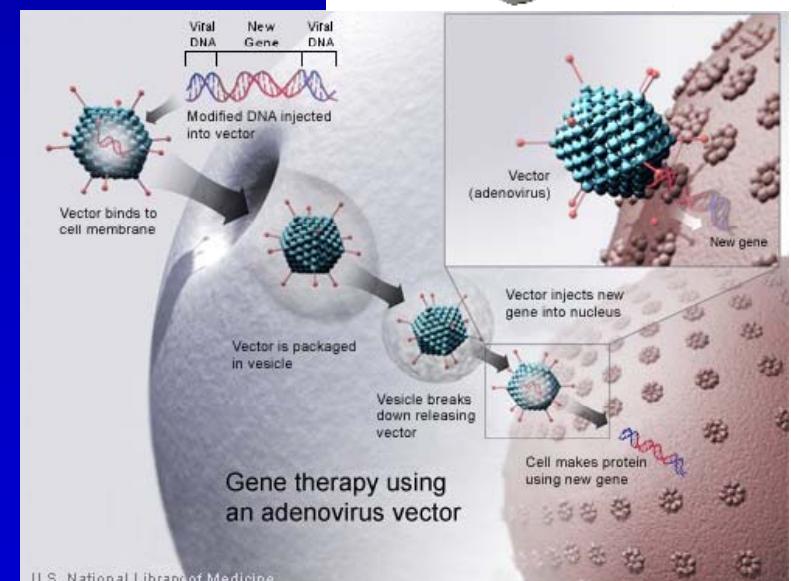
Two General Strategies in Using Genes for Repair

- Gene therapy
 - Replacement, reduction, or compensation for an (inborn) genetic error
 - Easy in the lab, tough in the clinic
 - Issues of correct targeting and regulation
 - Permanent alteration to correct fatal disease
- Gene medicine
 - Short term activation or repression of a gene to promote innate repair
 - Use of genes and/or cells that act transiently



Gene Medicine for Wound Healing: Strategies

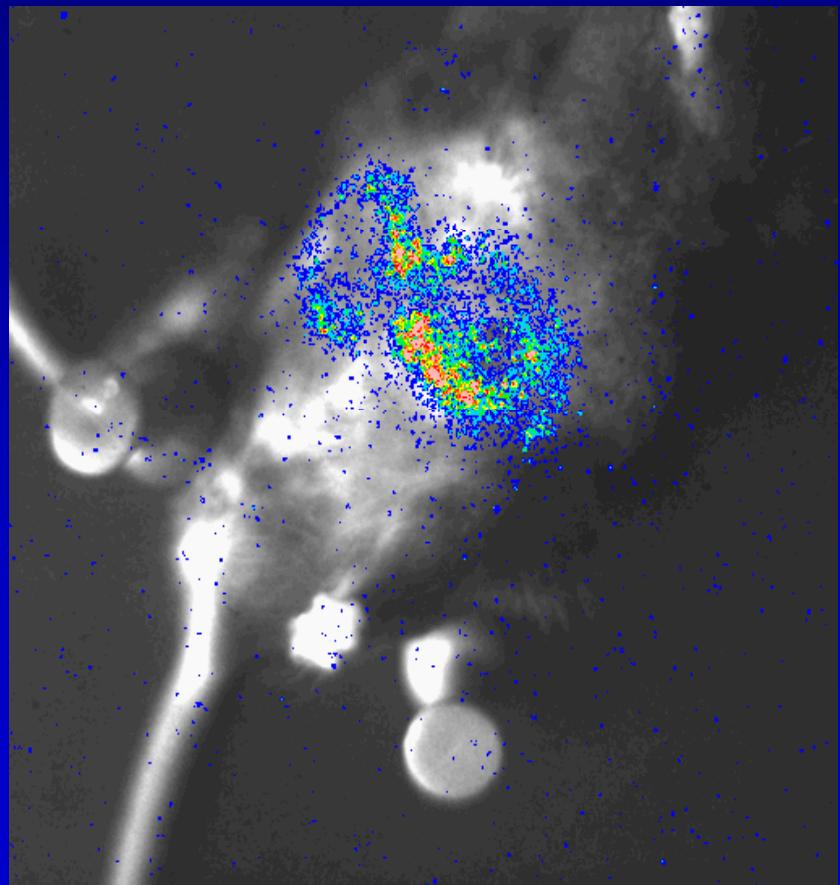
- Naked DNA (plasmid)
 - Easy to manufacture, hard to get into cells
 - Physical and chemical delivery systems
 - Gene gun: surface-dependent
 - Incorporation into gels, films, biomaterials, liposomes, nanoparticles
 - Fast, inefficient, inexpensive
- Viruses - nature's gene delivery systems
 - Adenovirus - efficient, transient
 - Retrovirus -
 - permanent introduction of genes
 - Useful for genetic engineering of tissue engineering products
 - Can be used in conjunction with controllable genes
 - Topical activation
 - Systemic activation
 - Production costs and immunologic issues





Mouse Transfection with Luciferase by Gene Gun/Particle Bombardment/ Biolistic Transfection

- Gene gun loaded with *luc* expression vector
- Introduced into epidermis at two pressures
- Visualized with topical luciferin in DMSO @ 2d





A photograph of a surgical procedure in progress. A surgeon in green scrubs and a mask is focused on the patient's abdomen, which is partially shaved and has a bright orange surgical drape. To the left, another surgeon stands by a table covered in a green cloth, which holds various surgical instruments in sterilized containers. In the foreground, a blue tray is filled with a large quantity of surgical instruments, including forceps, scalpels, and needles. The lighting is dramatic, with strong highlights from the surgical lights.

Wound Care: ambulatoriale o ospedalizzazione