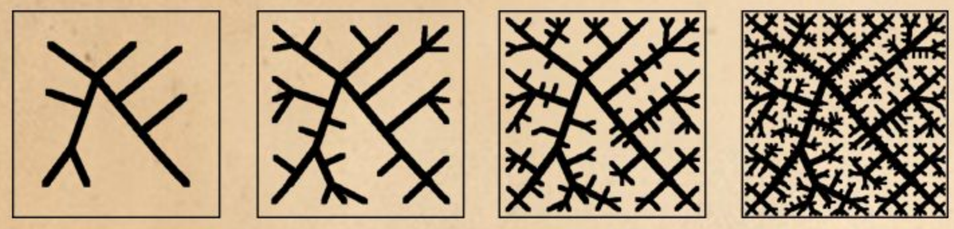
Marc E. Gottlieb, MD, FACS

A Professional Corporation

PLASTIC & RECONSTRUCTIVE SURGERY

Board Certification ••• ••• ••• *Plastic Surgery* ••• *Hand Surgery* ••• *General Surgery*



Specializing in the treatment, reconstruction, and management of
Acute and chronic wounds • Diseases and defects of the soft tissues • Injuries, diseases, and defects of the hand and extremities • Defects of the head and trunk

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INTEGRA ARTIFICIAL SKIN
Understanding its Extraordinary Clinical Results and Economic Efficiencies

Original presentation December 14, 2005, Bethesda, MD, at CMS. Sponsored by Integra Life Sciences.

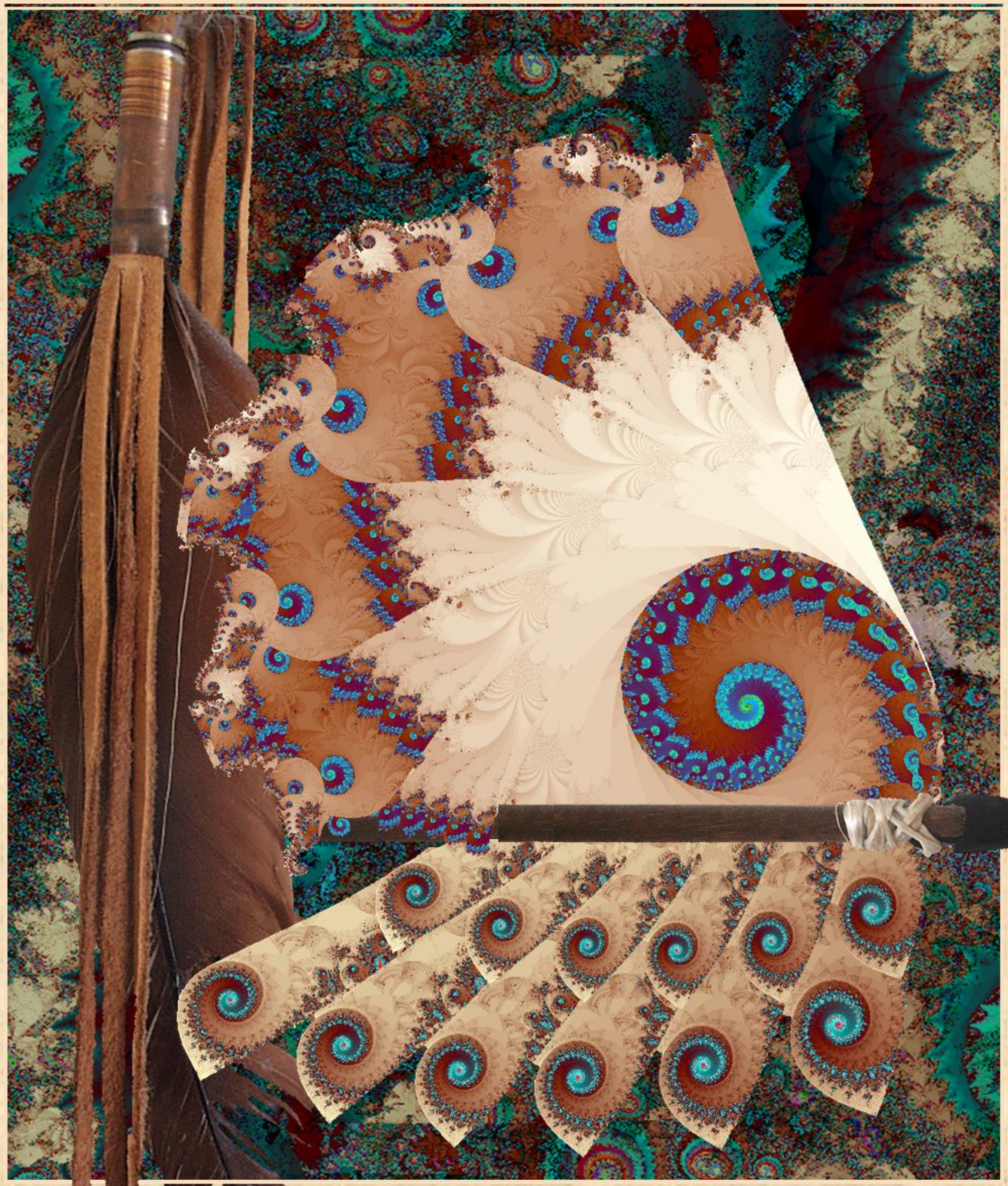
December 13, 2005 – This presentation is not yet annotated.

INTEGRA ARTIFICIAL SKIN

Understanding its Extraordinary Clinical Results and Economic Efficiencies

Marc E. Gottlieb, MD, FACS

Superior Technology - Superior Results



INTEGRA

and the Medicare patient

Presented by

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2003

INTEGRA

is a unique implant
which reconstructs healthy skin

there is no substitute,
nothing comparable

it solves difficult problems
easily, at low risk and utilization

it saves limbs,
lives, and livelihoods

it saves large sums of money
in the care of individual patients

it fits perfectly into to the burgeoning
infrastructure of outpatient wound care

superior to conventional paradigms of care

effective, dependable, superior results,
with less risk and less cost

2005

INTEGRA

Main Points

Integra remains a unique product

it is a new paradigm of wound repair

**it solves difficult problems
that have no other good solution**

**it is superior to and supplants prior
art – such as flaps and amputations**

used for difficult, risky problems

requires technical skill and expertise

BUT

low cost and complications

ideal for outpatient management

1 - INTEGRA IS A NEW PARADIGM OF WOUND REPAIR - 1

The Chronic and Pathological Wound

Healthy wounds

benign, trauma or incidental, acute, without persistent injury

wound healing competent

Healthy wounds can heal by themselves, or with basic surgery (simple repair and grafts)

Pathological wounds

morbid, due to active disease, chronic, continuing active injury

wound healing incompetent

Pathological wounds may require remote flaps of healthy tissue; for some, surgery must be avoided.

Chronic venous ulcer, factor V Leiden, obesity

DM, hand atherosclerosis, open tendons and joints

Severe rheumatoid and atherosclerosis

Atherosclerosis, open tibialis tendon

In these examples, conventional options are risky and prone to fail.

ARTERIAL
VENOUS
DIABETES
NEUROPATHY
PRESSURE
IMMUNOPATHIC
COAGULOPATHIC
HEMATOLOGICAL
DERMATOSES
PANNICULOPATHIES
TOXIC - METABOLIC
RADIATION
MECHANICAL
INFECTIOUS
CANCER
MIXED

Integra Versus Conventional Surgery

Integra: Successful wound surgery when other options fail

Wound Closure Surgery - 3 Classic Paradigms

PARADIGM #0:
NATURAL CONTRACTION

The body is programmed to heal. If the subject is healthy, a wound will close by the natural process of contraction and epithelialization.

PARADIGM #1:
SIMPLE REPAIR

Simple repair is the reduction and approximation of wound margins. Physiological wound healing then amalgamates the coapted edges. Most surgery and trauma is closed this way.

Wound Closure Surgery - 3 Classic Paradigms

PARADIGM #2:
GRAFTS

A graft has no anatomical attachment to the host, no circulation of its own, and cannot live independently. Skin grafts are used mainly for convenient wound closure in a healthy wound.

PARADIGM #3:
FLAPS

A flap maintains an anatomical attachment to the host, carrying its own circulation. Flaps are used when normal tissue qualities are needed, when the target has exposed structures, and when the target is wound healing incompetent.

Direct repair: Simple repairs succeed when host and target wound are healthy and wound healing competent.

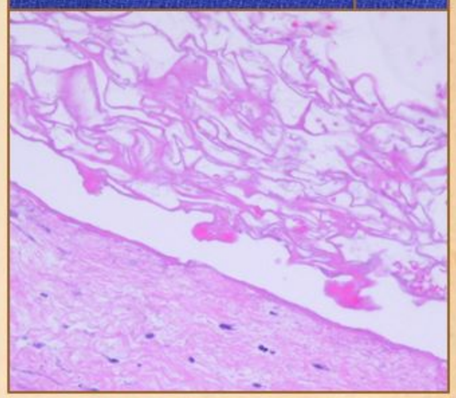
Grafts: Likewise, grafts depend on a host and target wound that are healthy and wound healing competent.

Flaps: If the target wound is pathological or incompetent to heal, but the host is healthy, then healthy flaps succeed.

All have one thing in common: They depend on normal wound healing.

Integra – The Material

A Bilaminar Surface Implant



Layer 1 **Collagen-GAG Matrix**
(a sponge of type 1 collagen & chondroitin-C)

Layer 2 **Silicone rubber "epidermis"**
(temporary, eventually replaced with autogenous epidermis)

Integra has remarkable properties

High quality artificial skin.

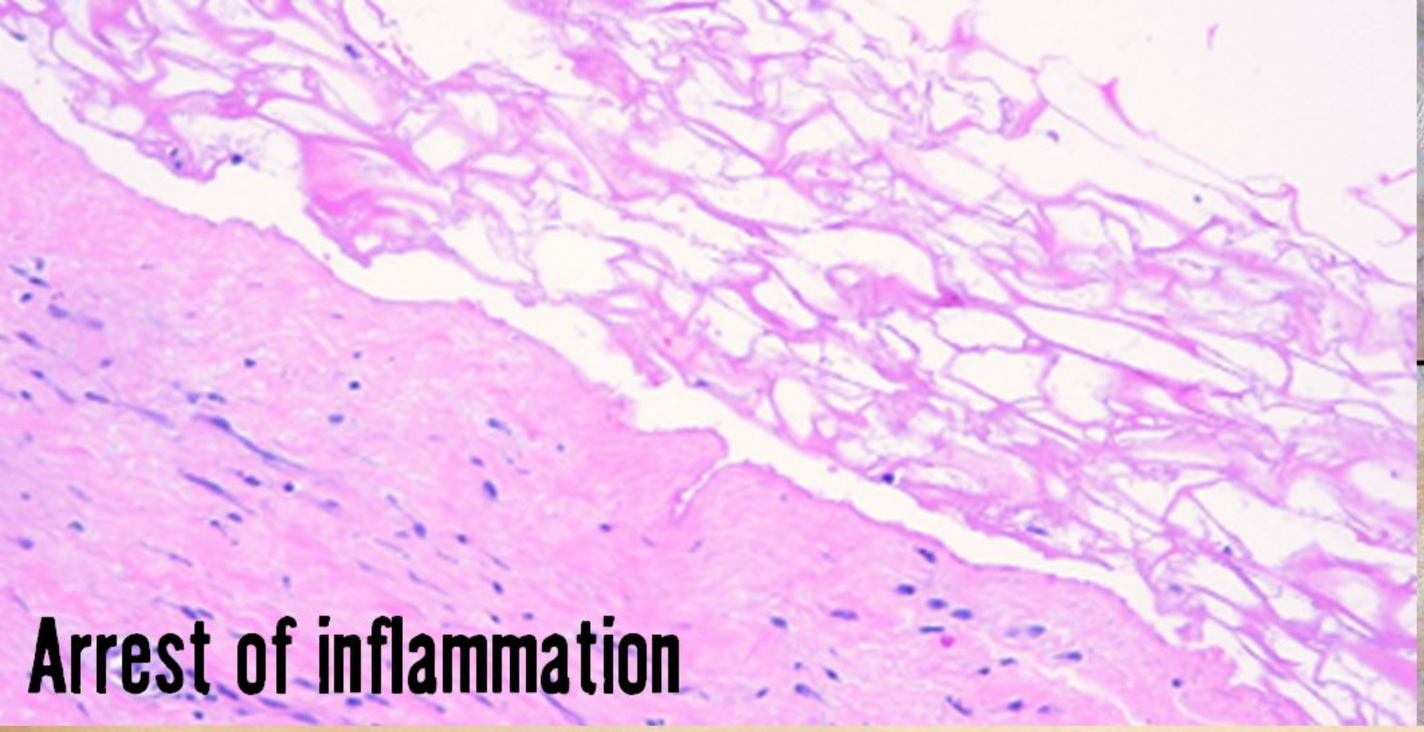
Short effects:

Completely suppresses inflammation & pathological wound dynamics → necrosis & ulceration cease.

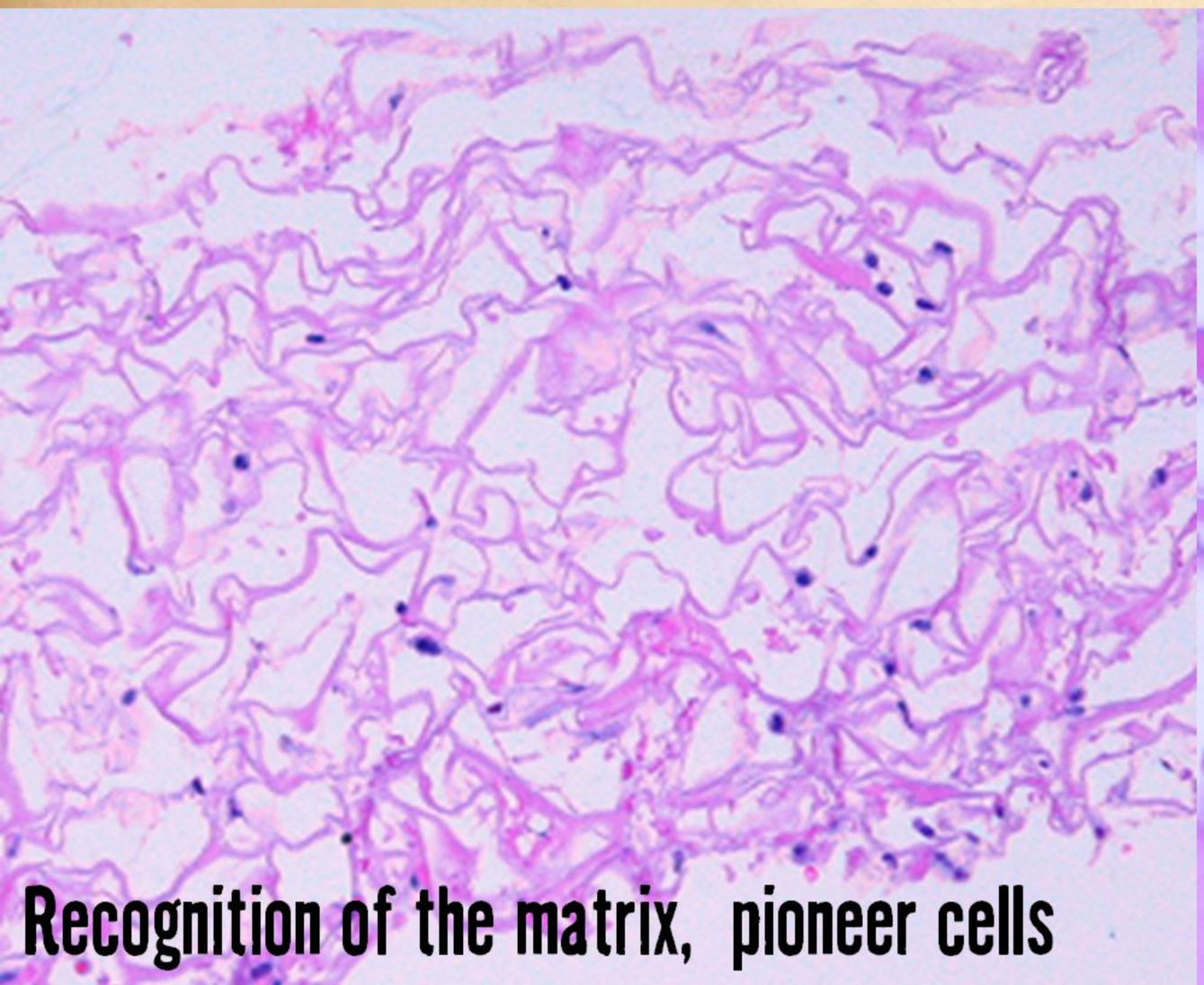
Long effects:

No inflammation → no wound healing → no scar.
Induces embryonic dermatogenesis.

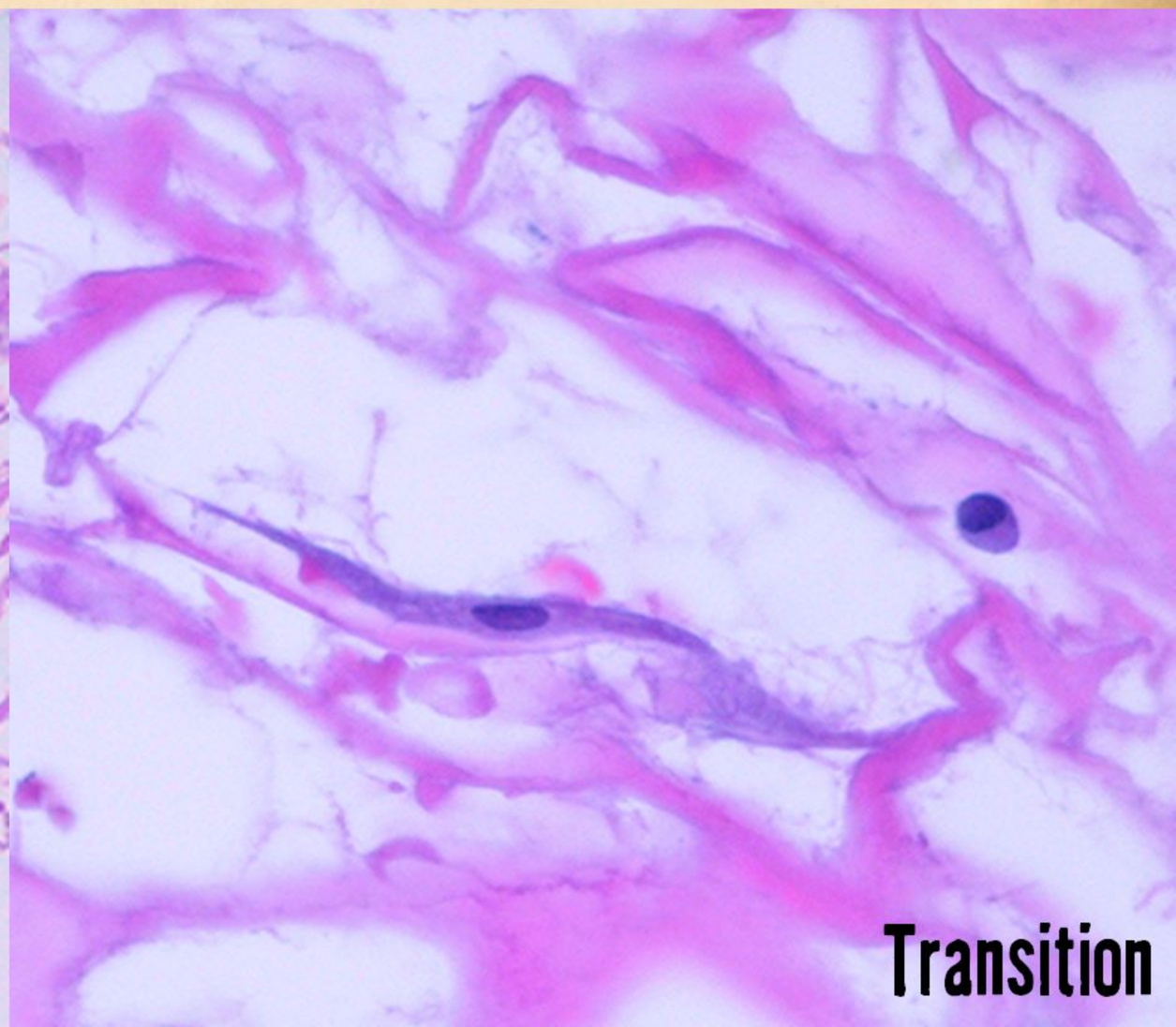
Rheumatoid arthritis, factor V Leiden, low proteins C & S. Refractory. Complete arrest of inflammation with Integra.



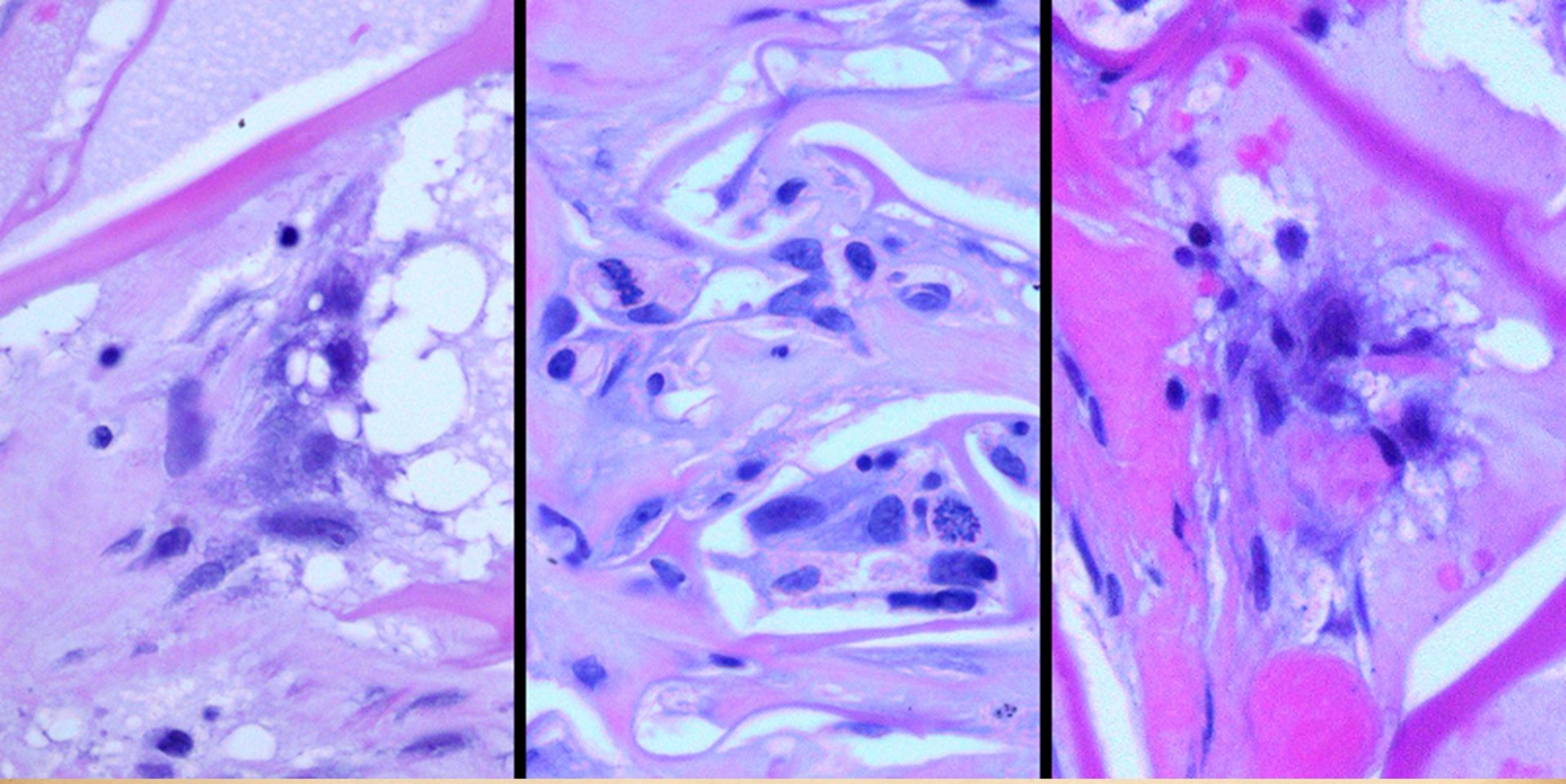
Arrest of inflammation



Recognition of the matrix, pioneer cells



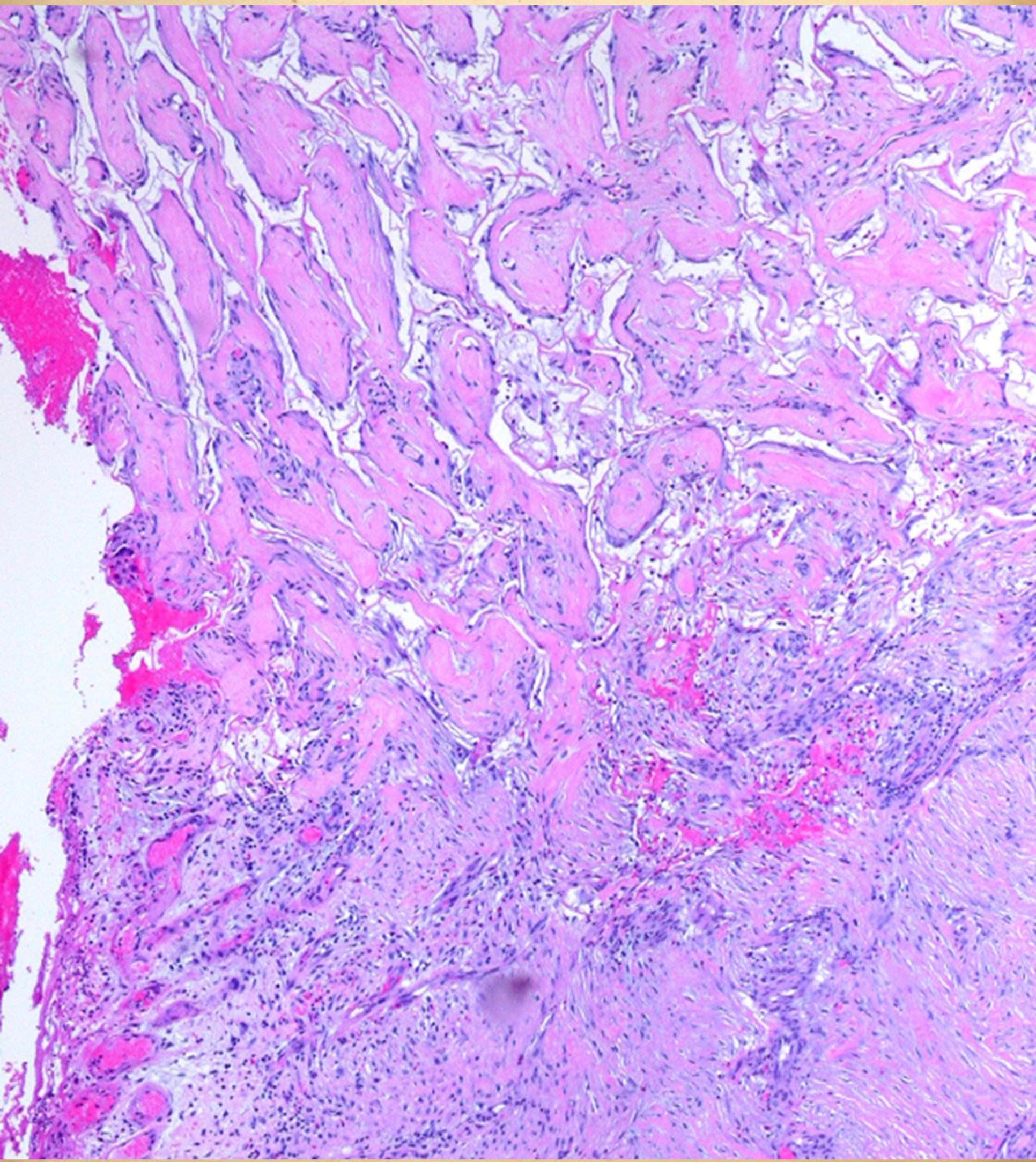
Transition



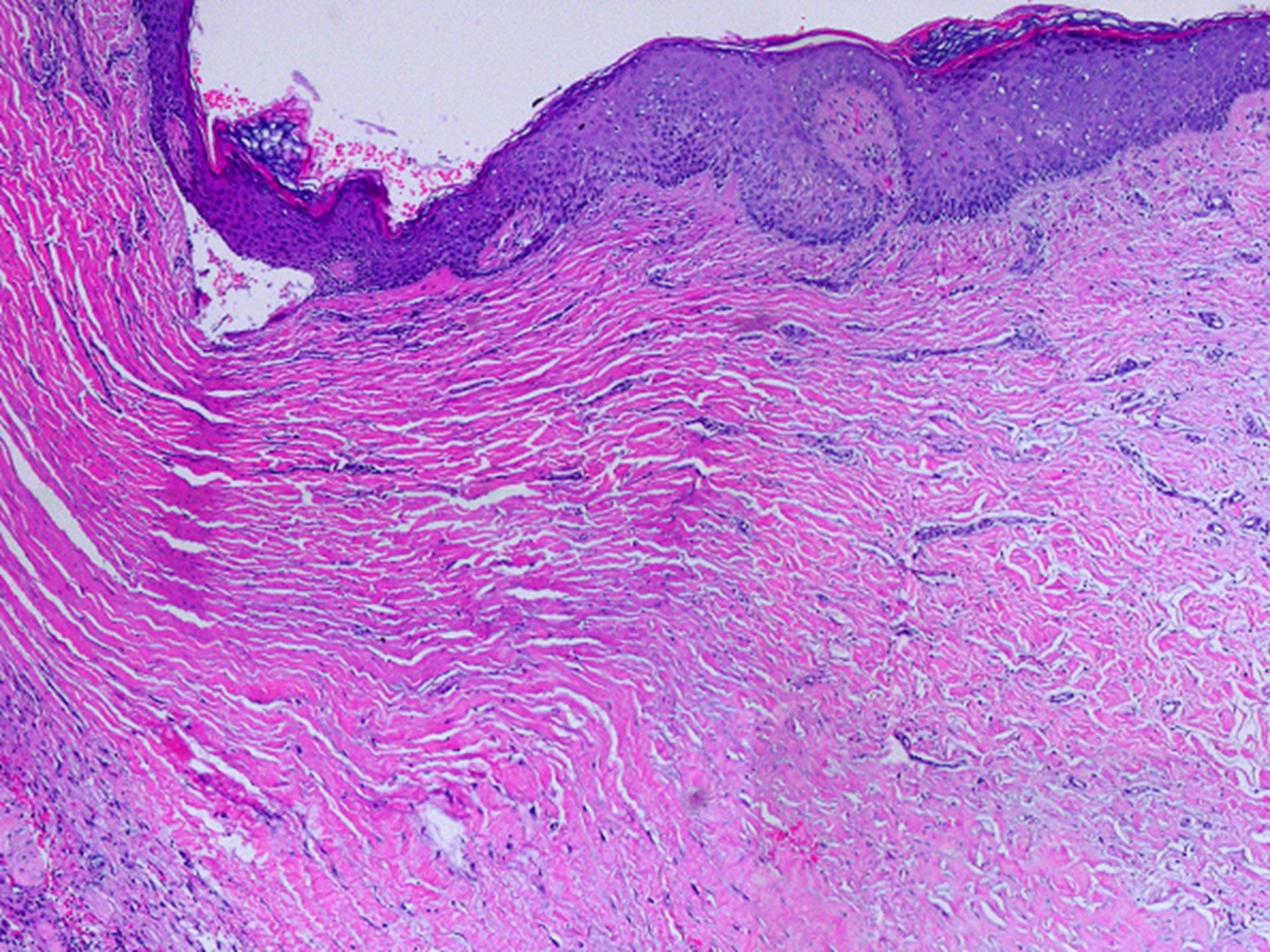
Syncytial fibroblasts & clusters

(The embryonic dermatoblast)

Integra Histogenesis - versus - Inflammatory Wound Healing



Integra Histogenesis - versus - Inflammatory Wound Healing



A FOURTH INDEPENDENT PARADIGM OF SURGERY

In-Situ Tissue Engineering

Integra is a distinct new paradigm of surgical wound closure, in-situ tissue engineering.
Unlike repairs, grafts, flaps, it does not depend on normal wound repair.
On the contrary, it suppresses normal repair, initiating embryonic histogenesis. It succeeds where conventional modalities fail.

Not an Alternative, but the Indicated Option

In many cases of problem wounds, Integra is the preferred option, because flaps and grafts will not work, and also because it can be the most suited modality:

superior results with less risk.

Integra:
Successful when other Options Fail

There are problem wounds that conventional surgery cannot solve. There are times when flaps cannot be done or will not survive.

Then what ?

Persistent disease or inflammation prevent repair.
Integra is not alive, so it tolerates harsh conditions. It suppresses residual inflammation.

Local conditions will not support a graft.
Not alive at the outset, it survives where grafts fail.

Flaps not large enough or may not reach the target.
Not autogenous; quantity, procurement irrelevant.

Illness and comorbidities make surgery too risky.
Placing Integra is simple, with no physiological tax.

Flaps can sacrifice useful parts and function.
No autogenous tissue donation.

Failed flaps waste anatomy and limit further options.
No autogenous tissues. No failures, no waste.

Inflammation and disease can threaten a flap.
Because it is not alive, tolerant, and suppresses inflammation, Integra is preferred in these conditions.

Vascular disease can kill a flap.
Circulation-independent, survives where flaps cannot.

Hematological disorders can kill a flap.
Not alive, tolerant of incidental pathology and injury.

Connective tissue disorders and wound pathologies will prevent healing or cause progressive ulceration.
Not only tolerant of incidental pathology and injury, Integra has a potent ability to withstand effects of connective tissue immunopathy and pathology.

Any disorder which caused the pathological wound will cause comparable problems for the repair.
Integra not dependent on normal wound repair physiology – suppresses repair, induces histogenesis.

Similar risks for the donor site, enlarging the problem.
No donor sites, no risk.

Risk of contractures after grafts.
Regenerates dermis, not scar. No contractures.

IN SITU TISSUE ENGINEERING WITH INTEGRA
A FOURTH PARADIGM OF SURGICAL WOUND REPAIR

Integra: Successful when other Options Fail

There are problem wounds that conventional surgery cannot solve.
There are times when flaps cannot be done or will not survive.

Then what ?

Understanding when a flap should be used, but cannot be used, is to understand when Integra should be used in lieu of conventional surgery.

A cure for chronic and pathological wounds.

Integra for chronic pathological wounds - Outcomes, by diagnosis

Diagnostic category (% of patients per category)	fully healed	> 2/3 healed	< 2/3 healed	failed
Macro-arterial	58	8	16	18
Immunopathic	74	16	5	5
Venous / lymphedema	88	---	6	6
Hypercoagulable	86	---	14	0
Mechanical / anatomical	88	12	---	0
Radiation / malignancy	72	28	---	0
Diabetes / neuropathy	0	20	40	40
Unknown	60	20	20	0
Micro-occlusive	100	---	---	0
Trauma / surgery	100	---	---	0
Granulomatous / infectious	50	50	---	0
Adjunct	100	---	---	0
Total	**71**	**10**	**10**	**9**

Integra used to close chronic wounds.

120 patients.

90%
of exposed bones, joints, tendons and organs were successfully closed.

If patients now recognized as poorly selected are excluded (extreme arterial insufficiency, and diabetic plantar ulcers), the success rate for healed wounds was 92%.

Gottlieb ME, Furman J: Successful Management and Surgical Closure of Chronic and Pathological Wounds Using Integra®. Journal of Burns & Surgical Wound Care, 3:2, 2004. (journalofburnsandwounds.com).

Gottlieb ME. Management of Complex and pathological Wounds with Integra. In: Lee BY, ed. The Wound Management Manual. New York, McGraw-Hill, 2004: 226-289. (ISBN 0-07-143203-5).

Understanding when a flap should be used, but cannot be used, is to understand when Integra should be used in lieu of conventional surgery.

64 m aorto-iliac occlusive disease

In each of these cases, conventional plastic surgery rules dictated a flap to close exposed essential structures, restore function, or salvage limbs.

In each, caveats of disease and local anatomy militated against flaps.

Because Integra can circumvent most of these exceptions,

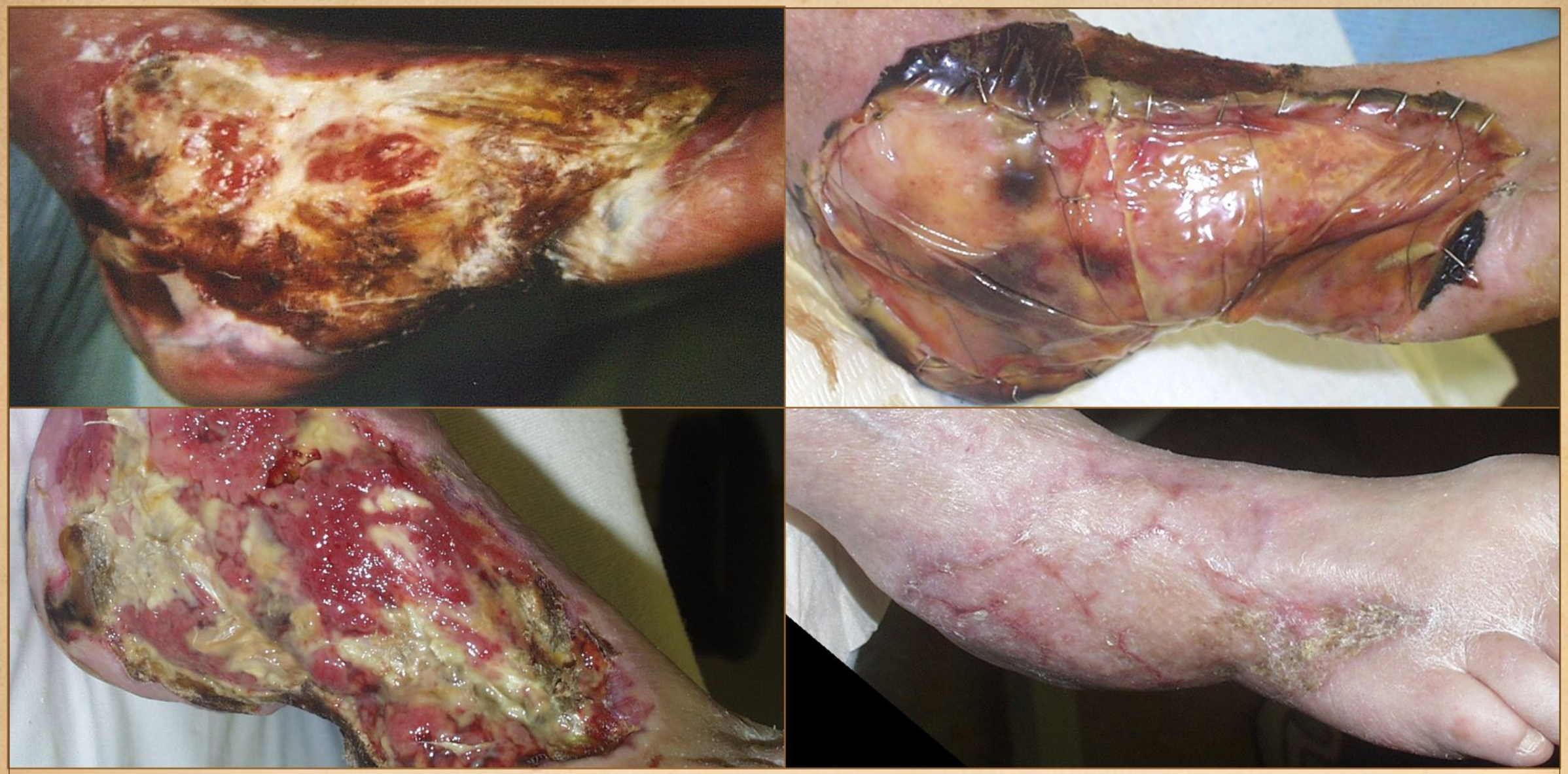
each case had a successful outcome by reconstructing skin with Integra.

42 f Pima diabetes, atherosclerosis

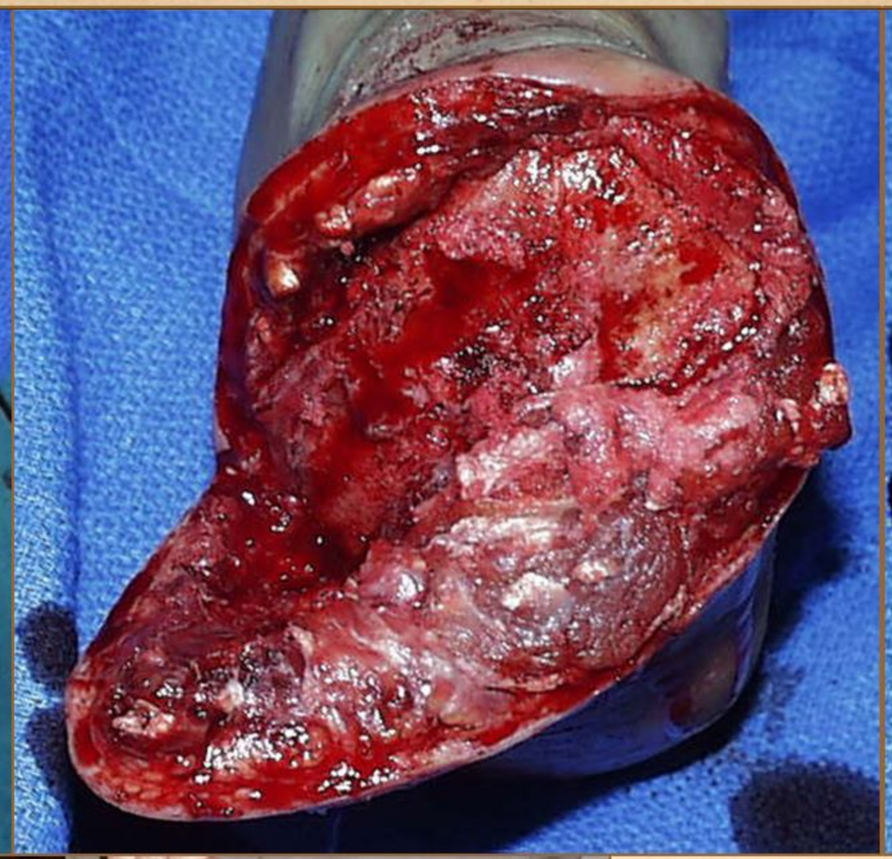
Conventional surgical options

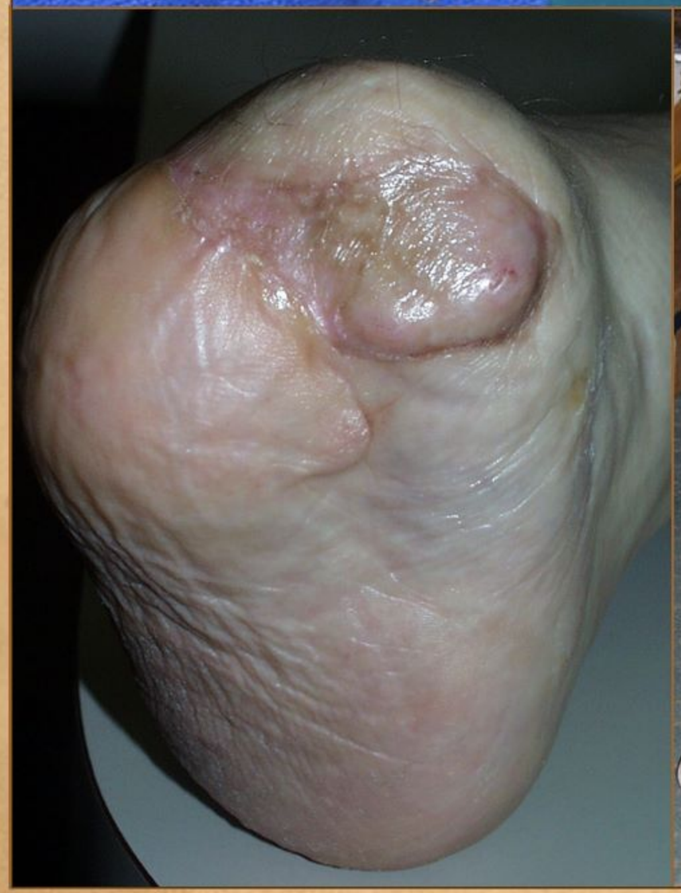
will not work,

and will make patient worse.



67 f ischemic infarction





73 m
embolic necrosis

58 m intra-arterial injection injury

53 m

diabetes

atherosclerosis

90 f
aso / pvod

84 f
diabetes
aso / pvod

60 m diabetes, atherosclerosis

2005
INTEGRA
Main Points

Integra remains a unique product

Integra is a new paradigm of wound repair – in situ tissue engineering.

It does not depend on normal wound healing.

It solves difficult problems that have no other good solution, especially those where wound healing is impaired or risks are high.

Success rate is very high for problems that other wise have dim prospects.

It is superior to and supplants prior art – such as flaps and amputations.

ARIMEDICA

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COMING UP NEXT

low cost and complications

ideal for outpatient management

resources required

INTEGRA

Administrative - Economic Issues

A PERFECT OUTPATIENT PRODUCT

Outpatient Use

Treat tough problems with low risks.

Get great results with low utilization.

Integra vs skin substitutes

Integra vs skin grafts

Effort and resources

Sizes and venues

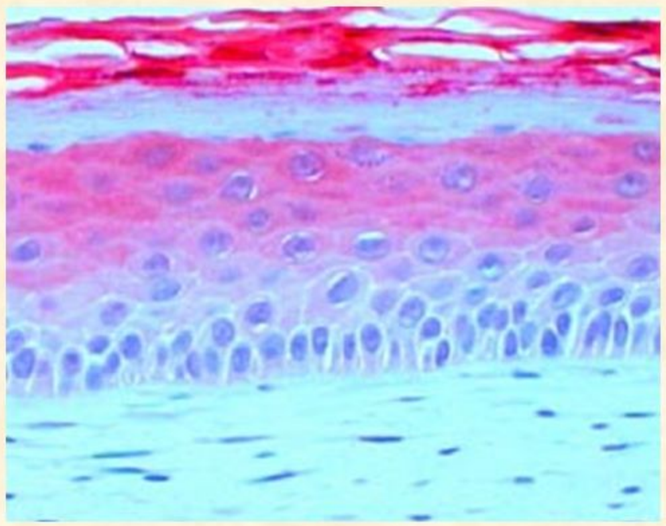
Integra for chronic pathological wounds
Inpatient versus Outpatient

Year	Total Integra patients	Number of IN-patients	Percent IN-patients
1996	4 (8)	3	75
1997	18	11	61
1998	10	5	50
1999	19	9	47
2000	16	4	25
2001	28	6	21
2002	12 (24)	0	0
Total	107	38	36

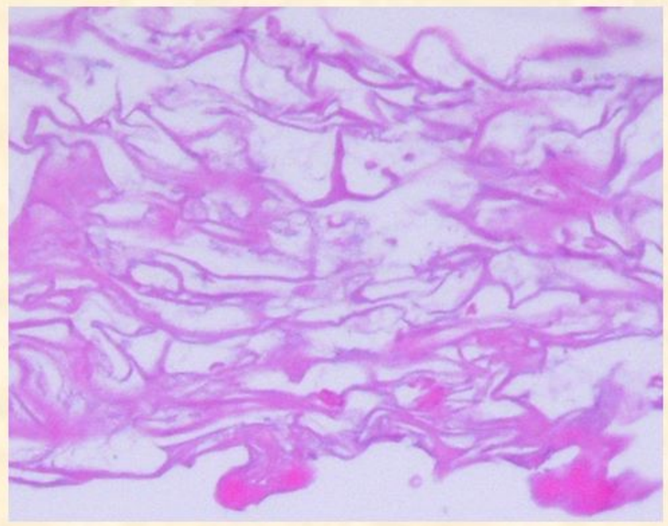
Gottlieb ME, Furman J: Successful Management and Surgical Closure of Chronic and Pathological Wounds Using Integra®. Journal of Burns & Surgical Wound Care, 3:2, 2004. (journalofburnsandwounds.com).

INTEGRA VS SKIN SUBSTITUTES

Apligraf
& Dermagraft
Allograft, etc.



Integra



Similarities

engineered bilaminate material

used for some aspect
of treating wounds

comparable cost **per unit**

Coding & reimbursement basis

Differences

living material
biological dressing
bio-pharmaceutical

small (many) units applied frequently
clinic / office service
not final nor definitive
inflated net costs

agent & accelerant of wound healing

Differences

non-living material
induces histogenesis
surgical implant

one (few) units applied once
outpatient surgery service
final, definitive, durable
predictable net costs

agent of skin reconstruction

Apligraf, etc.

Integra

TWO ENTIRELY DIFFERENT PRODUCT CLASSES

BOTH are exceptionally important to modern wound care
BOTH have different and distinct indications, methods, and outcomes

Differences

APLIGRAF and DERMAGRAFT
are used as pharmaceutical agents
to stimulate healing in
non-healing wounds

they are WOUND HEALING products

Differences

INTEGRA
is a histoinductive implant
which regenerates normal tissue
in lieu of injured or diseased tissues

it is a SKIN REGENERATION product

INTEGRA VERSUS SKIN GRAFTS

The technique of applying Integra is comparable to skin grafts.

**But, Integra is used for cases where skin grafts will not work -
used, in fact, for cases which are already the most morbid and indicated for flaps.**

**So, even though the technique seems somewhat low key,
it is in fact demanding, and good results are in the details.
Post-operative aftercare is much more involved than ordinary skin grafts.**

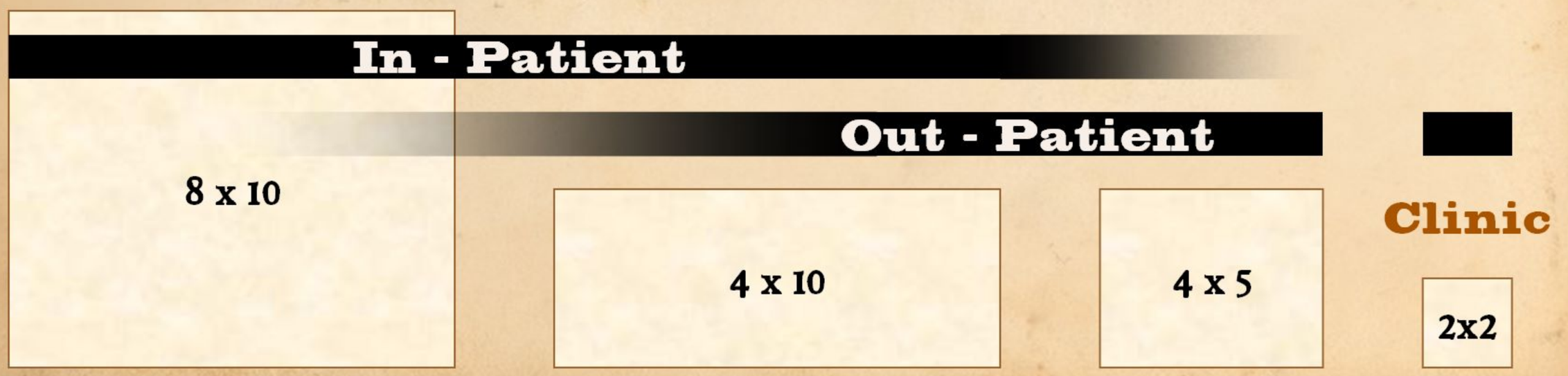
INTEGRA & OUTPATIENT CARE

Acute
Larger
In-patient status & surgery

burns
degloving
necrotizing fasciitis
major tumor resection

Chronic and pathological
Smaller
Outpatient surgery

the various diagnoses
discussed here



INTEGRA & OUTPATIENT CARE

With much of modern wound care,
the goal is to keep patients OUT of the hospital.

Concerning chronic wounds . . .
modern medical socioeconomics have forced us to develop the best care, resources, resource utilization, and results by keeping patients in clinics, offices, extended care facilities, and home – anywhere but the acute general hospital.

INTEGRA

Complex difficult problems
Great durable results
Outpatient
Efficient safe care
Economically advantageous

INTEGRA, CHRONIC WOUNDS & OUTPATIENT CARE

Integra's ability to protect a wound, control inflammation, suppress normal wound repair and scar, induce embryonic histogenesis, conduct histogenesis across gaps, withstand or tame disease, and do so with no risk to the patient is a set of features unparalleled among surgical and wound products.

A method of in situ tissue engineering, Integra is a genuinely new paradigm of wound surgery. Of equal rank to flaps and grafts, its biological properties, safety profile, and practicality make it preferred for many problems. This is especially true for chronic pathological wounds, where conventional repair, grafts, and flaps fail or are ineligible, and Integra succeeds, often with superior results.

Furthermore, Integra incurs no donor sites nor risk to the patient, and a reconstruction for a chronic wound can be managed almost entirely as an outpatient, preserving activity and lifestyle. A versatile surgical tool with unique properties and safety, Integra has become a preferred method of closing chronic and pathological wounds.

Integra belongs in outpatient venues,
and its use there should be encouraged.