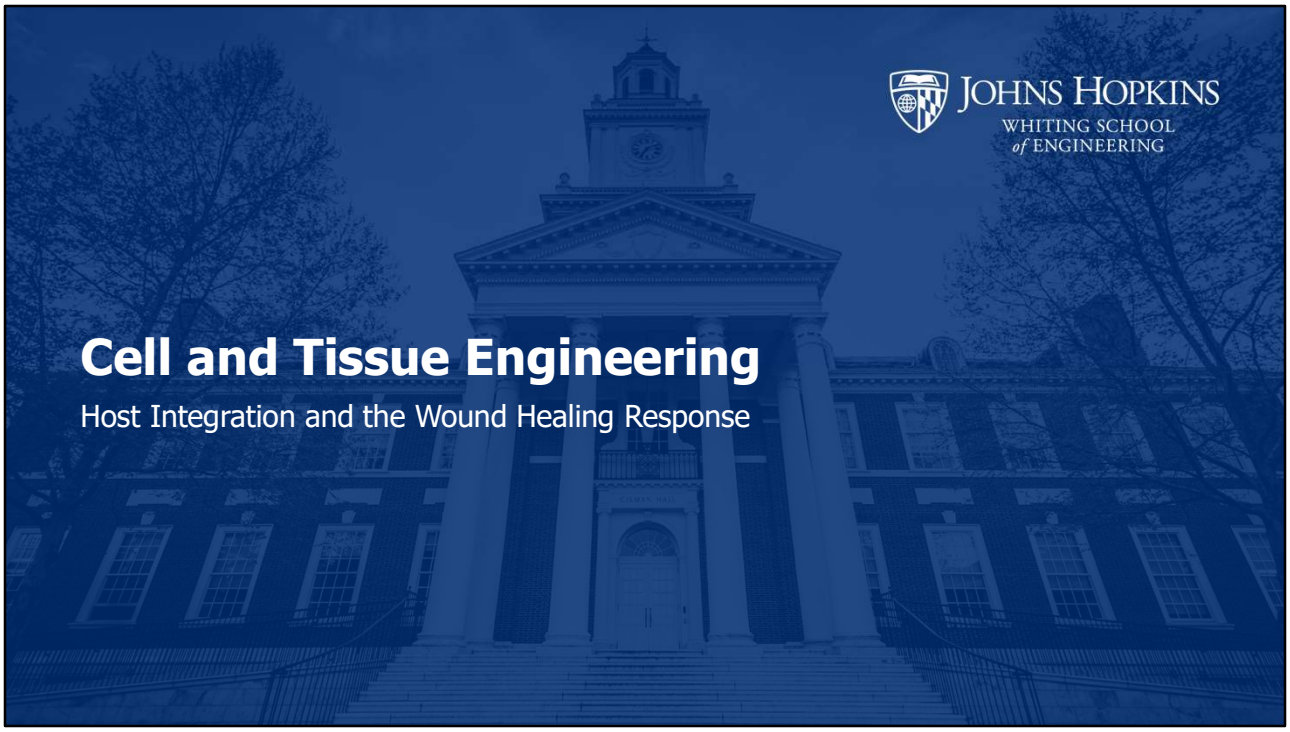
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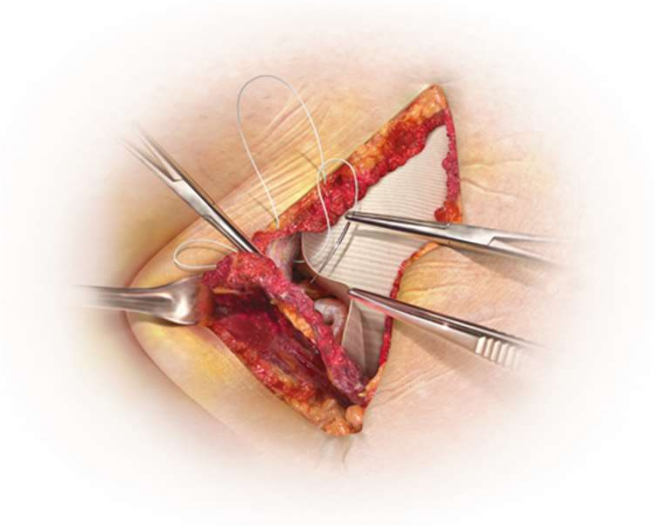
WHITING SCHOOL
of ENGINEERING
Cell and Tissue Engineering
Host Integration and the Wound Healing Response

How Do We Integrate a Tissue Engineered Product?

Wound healing

Angiogenesis

Immune response



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http://www.goremedical.com/dualmeshplus/

So far, we have discussed biomaterials – properties, types, attributes and tailored functionality.

Here we will discuss considerations for **integration** of that tissue engineered **product** into the **patient**.

What do we need to be thinking about?

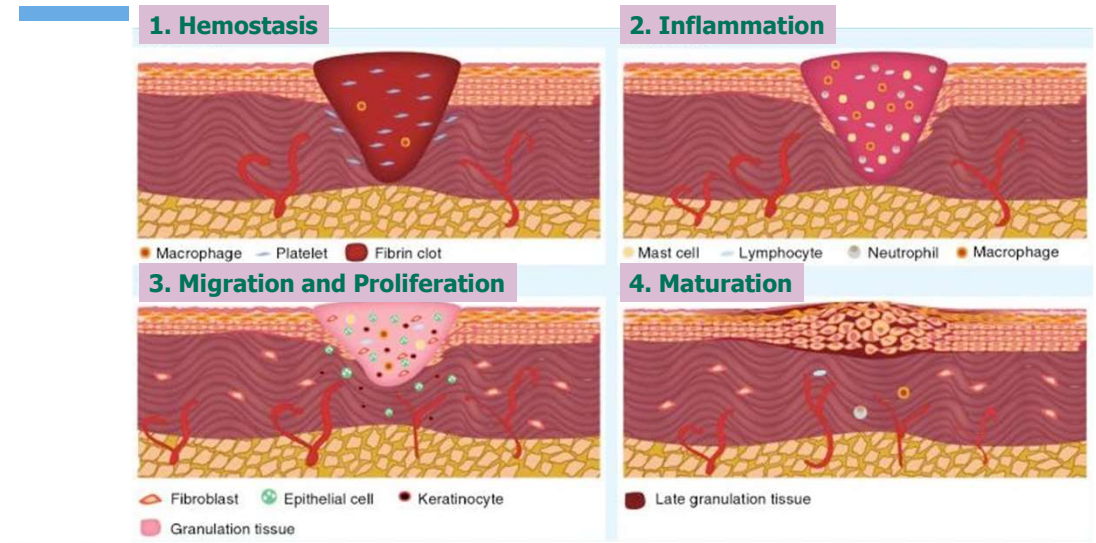
With surgical intervention there is always **a wound healing response** –from the fact that you must create a wound to place the product.

This image is showing a product from **Gore** (as in goretex) that is used to repair intraperitoneal hernias. IN order to place the product a **large** surgical site is used opening layers of skin and muscle.

To close the wound, the body will initiate a wound healing response which will include angiogenesis (that is, the growth of new blood vessels from existing vessels) and an immune response from the body.

As a tissue engineer you can intervene in any of these multicellular processes at a variety of levels to improve host **acceptance** and **response** to the product.

The Wound Healing Response – Four Phases



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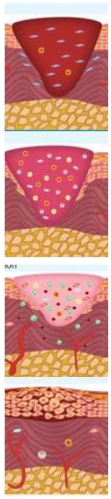
http://www.medscape.com/viewarticle/782469_2

In module 4 we looked the basics of the wound healing response when we discussed tissue dynamics including tissue homeostasis, repair and formation.

As a reminder, wound healing includes 4 main phases **Hemostasis**, **Inflammation**, **Migration**/proliferation and **maturation**. We'll briefly review these phases here

The Wound Healing Response - Timing



1. Hemostasis – seconds to minutes
2. Inflammation – minutes to days
3. Migration and Proliferation – days to weeks
4. Maturation – weeks to year

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http://www.medscape.com/viewarticle/782469_2

These phases each get progressively longer - starting with just seconds to minutes for hemostasis and ending with up to a **year** or more for full **remodeling** and **maturation** of the tissue.

In **hemostasis** the goal is to stop the bleeding through **clot** formation and **constriction** of damaged and leaking blood vessels

Following hemostasis, **inflammation** sets in.

The Wound Healing Response – Signs of Inflammation

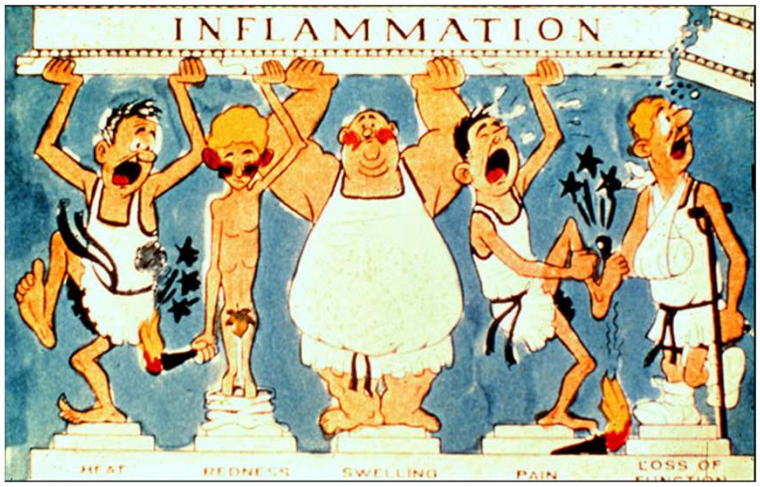
2. Inflammation – minutes to days

Calor

Rubor

Tumor

Dolor



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The wound is now described by **cardinal** signs of inflammation –**calor** (heat) **rubor** (redness), **tumor** (swelling), and **dolor** (pain). These signs have been known for centuries.

Sometimes in severe cases loss of tissue function is also noted as a fifth sign of inflammation.

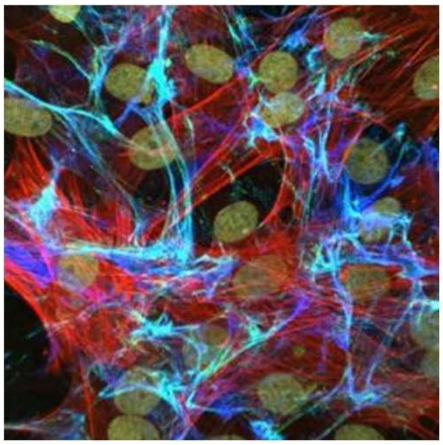
Dilated blood vessels increase the red appearance, and bring increased flow and heat to the injury site.

-- once the bleeding is stopped -- Higher permeability of these blood vessels leaks plasma into the wound site, leading to swelling. This swelling presses on nerves, and along with other mediators, is responsible for the pain felt in the wound.

During all of this inflammatory cells find their way to the wound cleaning debris and releasing factors to promote proliferation and migration of other cell types.

The Wound Healing Response – Migration and Proliferation

3. Migration and Proliferation – days to weeks



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http://phys.org/news117116139.html

This brings us to phase 3 where fibroblasts grow in number and begin the work of rebuilding the connective tissue through production of a provisional matrix.

Epithelial cells at the surface of the wound also proliferate to cover the open space while myofibroblasts pull the edges of the wound together.

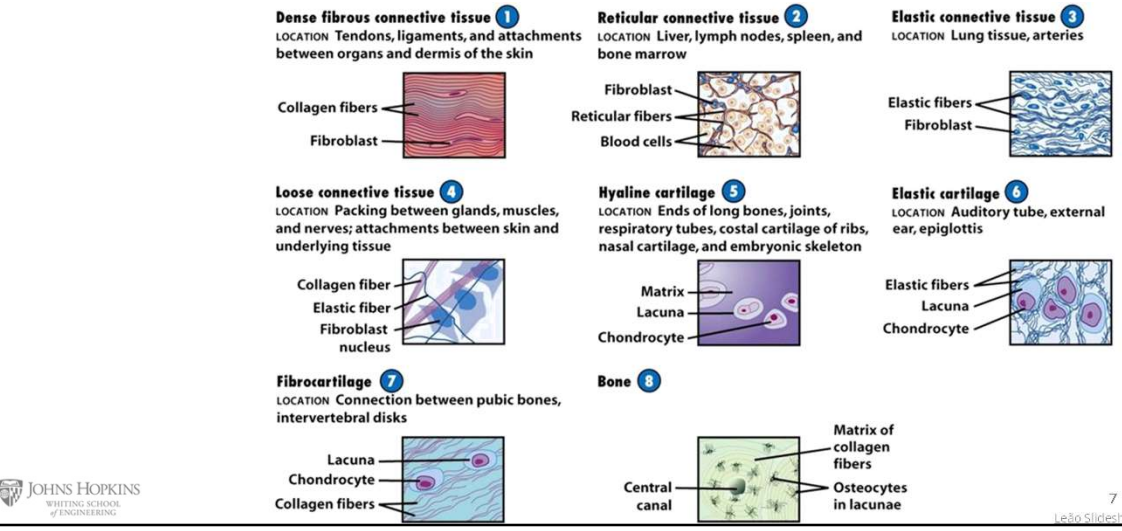
This fluorescent image shows you **fibroblasts** in red moving around the disorganized provisional matrix should in **blue**.

Overtime the wound will mature and remodel. Scars will **flatten** and become less apparent as unnecessary blood vessel get **pruned** back.

In the end the repaired tissue rarely recovers the mechanical properties it had prior to the injury.

The Wound Healing Response - Maturation

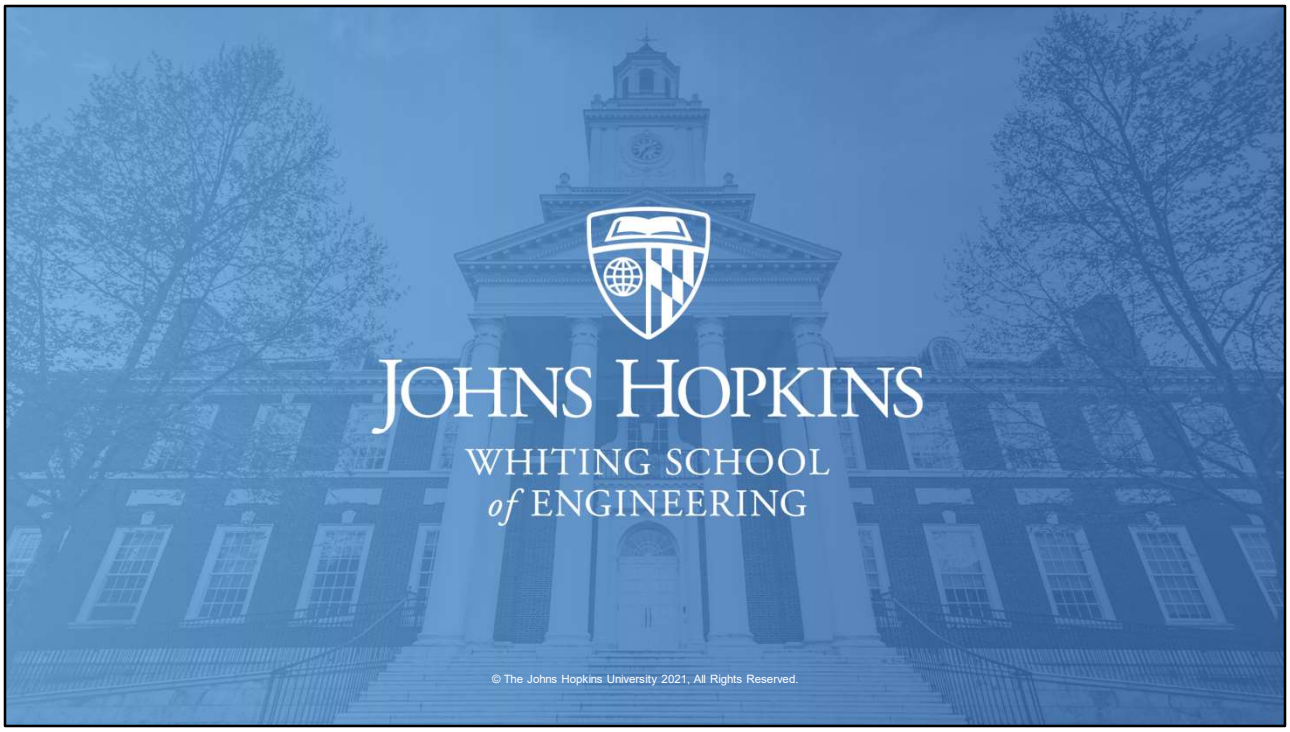
4. Maturation – weeks to year



Maturation is a slow ongoing process that takes weeks to a year. This process is different for each tissue type because each has a unique mature state, which you can see in this graphic showing the matured tissue pattern for different tissue types.

Each cell type has a different period of time to set up shop in the tissue again, and may never reach the organization or degree of function from before the injury.

For example, bone will slowly deposit and then be resorbed and then deposited again to align the structure to best carry the forces loading onto that bone.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