

### Introduction

Our sphere templating technique permits fabrication of biomaterials with precision control of key pore structural dimensions. We have found that these unique materials have potent pore size-dependent pro-angiogenic properties. We refer to them as STAR Materials (Sphere-Templated Angiogenic Regeneration). STAR Materials offer promising solutions to many current medical problems.

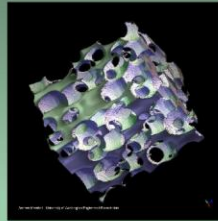


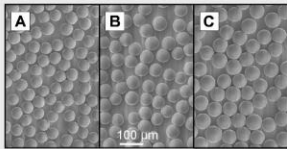
Fig. 2. 3-D reconstruction of STAR scaffold with 90-µm spherical pores created by automated reconstruction of serial sections via Digital Volumetric Imaging (DVI).

## COMMERCIAL APPLICATIONS

Research and development of STAR Material was performed by University of Washington Engineered Biomaterials (UWEB), with support from NSF, NIH, and USAMRAA.

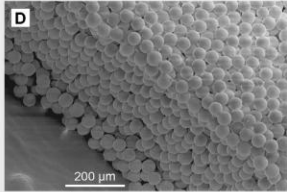
### Fabrication Summary: The Keys to "6S"

↓ **Sieve** polymer microspheres to uniform size fractions.



↓ **Shake** with ultrasonic agitation to pack beads.

↓ **Sinter** into fused-bead wafer by heating. The neck size between the beads is controlled by the duration of sintering.



↓ **Surround** with polymer precursor. Fluid is wicked into the interstitial space via capillary forces.

↓ **Solidify** by polymerization.

↓ **Solubilize** microsphere template. Cross-linked network of interconnected spherical pores network remains.

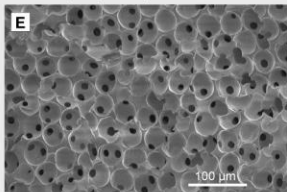


Fig. 1. (A) 50-µm beads. (B) 55-µm beads. (C) 60-µm beads. (D) Pore template of fused 60-µm beads. (E) Porous STAR hydrogel cast with pore template shown in (D).

### Implanted Biosensors: Promoting Angiogenesis to Overcome the Foreign Body Response

#### The Problem:

Implanted medical devices such as glucose sensors and electrodes cannot function for longer than a few days because the foreign body response quickly encapsulates the device with a layer of dense fibrous tissue, preventing electrical and chemical communication with the surrounding tissue.

#### Our Solution:

STAR Materials have been shown to have potent pore size dependent pro-angiogenic properties. If an implanted biosensor is encased in a porous sleeve of STAR Material, the resulting capsule is thinner, looser, and more vascularized, enabling sustained communication with the rest of the body. Figure 3 shows the effect of STAR Material on capsule tissue.

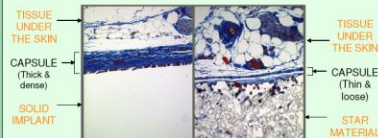


Fig 3. Silicone STAR material elicits a thinner, looser capsule (stained blue) when implanted under the skin of mice.

Fig. 4 shows mouse tissue sections stained for blood vessels (stained dark brown). The vessel density is increased dramatically when the pore size is optimized, as in panel (A).

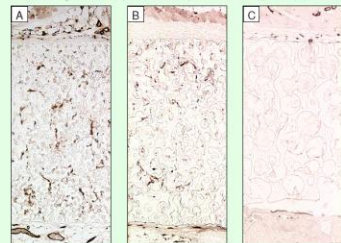


Fig 4. STAR materials of different pore sizes: (A) 35 µm, (B) 70 µm, (C) 160 µm.

Fig 5. Mock-up of implantable glucose sensor encased in a silicone STAR sleeve. The sleeve is partially cut away to reveal the electrode elements.



### Porous Catheter Cuffs: An Approach to Eliminate the Catheter Infection Problem

#### The Problem:

With all percutaneous devices (devices such as catheters that pass through the skin), the skin is unable to heal in a way that seals tightly around the device, leaving a gap at the skin-biomaterial interface that provides a gateway for bacterial invasion.

As a result, approximately 250,000 catheter-related bloodstream infections occur in U.S. intensive-care units each year, at an estimated cost to the healthcare system of \$25,000 per episode.

#### Our Solution:

STAR Material offers a promising solution to the catheter infection problem. Unlike existing available porous cuff materials, which have broad pore size distributions, STAR Material can be made with precisely controlled pore dimensions. STAR Materials with optimized pore size (on the order of cell dimensions) have been shown to give remarkable increases in skin cell ingrowth and anchorage, and to promote blood vessel development. The improved biointegration of epidermal cells and potent pore size dependent pro-angiogenic properties suggest that STAR Material can be used to eliminate infection at the skin-biomaterial interface.

A rafted organ culture model (with newborn human foreskin) was used in conjunction with sphere-templated polyHEMA and silicone STAR Material to study skin cell morphology at the percutaneous interface. Figure 8 shows epidermal keratinocyte (outer layer skin cell) integration into silicone STAR Material.

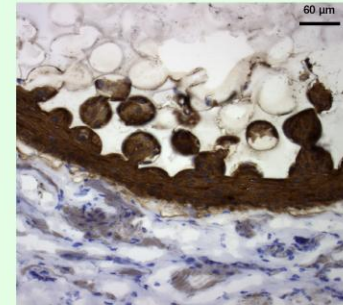


Fig. 8. Staining for keratinocytes at skin-biomaterial interface of silicone STAR Material with 60-µm pores after 6 days in organ culture.

### Tissue Engineering Scaffolds: A versatile material that shows promise for a wide range of tissue reconstruction applications, including skin, heart, esophagus, and pelvic prolapse.

#### The Problem:

Cells seeded inside scaffolds for tissue engineering have low survival rates due to a lack of access to oxygen and nutrients.

#### Our Solution:

Our pro-angiogenic STAR pore structures can be nested into the space between much larger pores. Figure 6 shows an example of a nested STAR pore structure comprising interconnected 500-µm spherical pores nested between interconnected 500-µm spherical pores. The larger pore network provides pathways for nutrient and oxygen exchange, while the network of smaller pores provides high surface area for cell attachment and angiogenesis. Figure 7 shows another type of nested STAR pore structure designed specifically for cardiac tissue engineering.



Fig. 6. STAR Material nested into the space between larger pores.

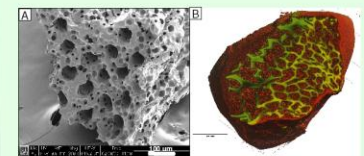


Fig. 7. (A) STAR Material nested into the space between parallel channels. In (B), this material (polymer stained green) has been seeded densely with cardiomyocytes (heart muscle cells, stained red) and imaged via digital volumetric imaging. These cells require both the large channels (for access to nutrient exchange) and the smaller-pored STAR pore structure (which provides surface area for anchorage and angiogenesis) to survive.