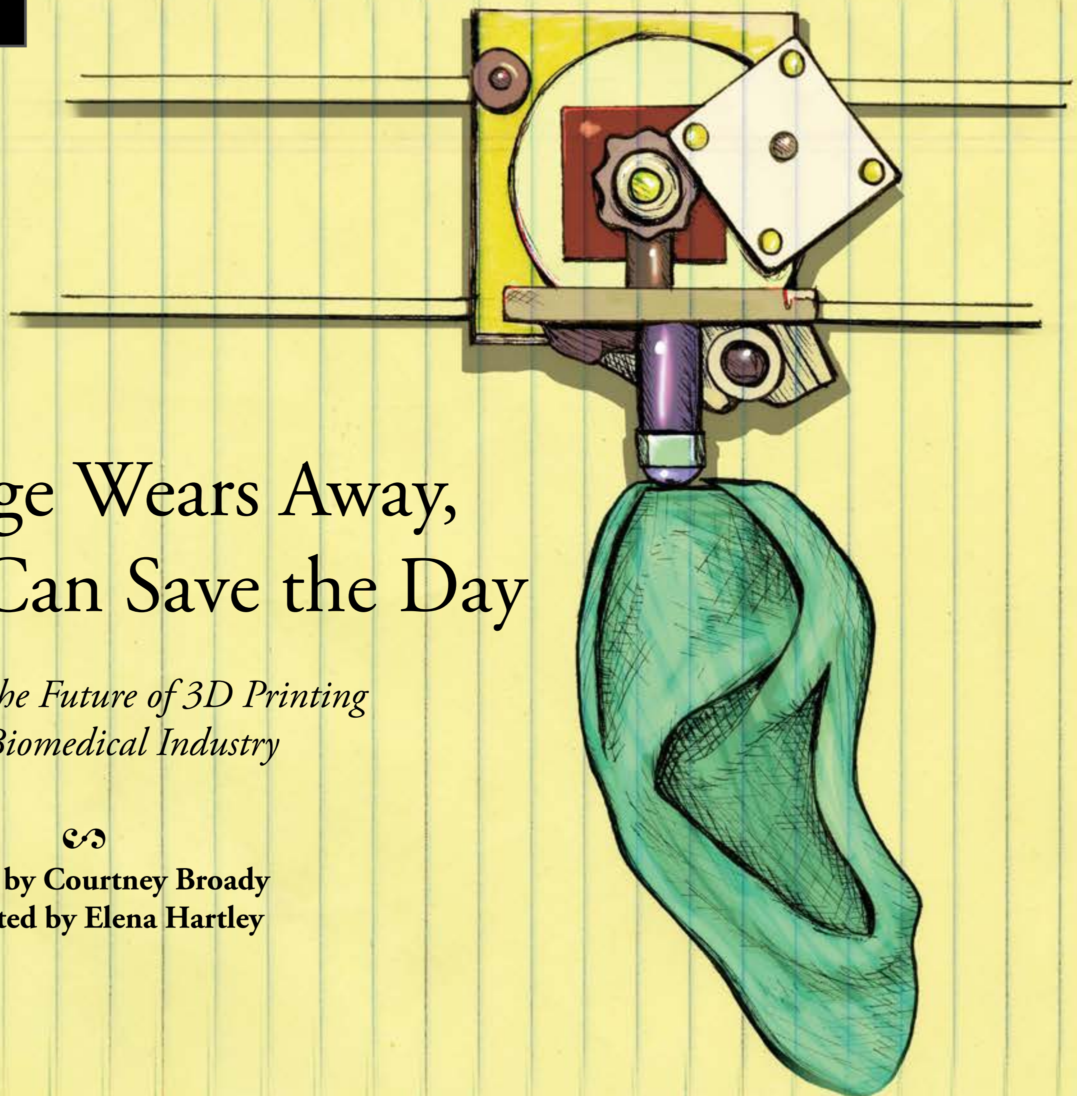

If Cartilage Wears Away, Hydrogels Can Save the Day

A Look into the Future of 3D Printing in the Biomedical Industry

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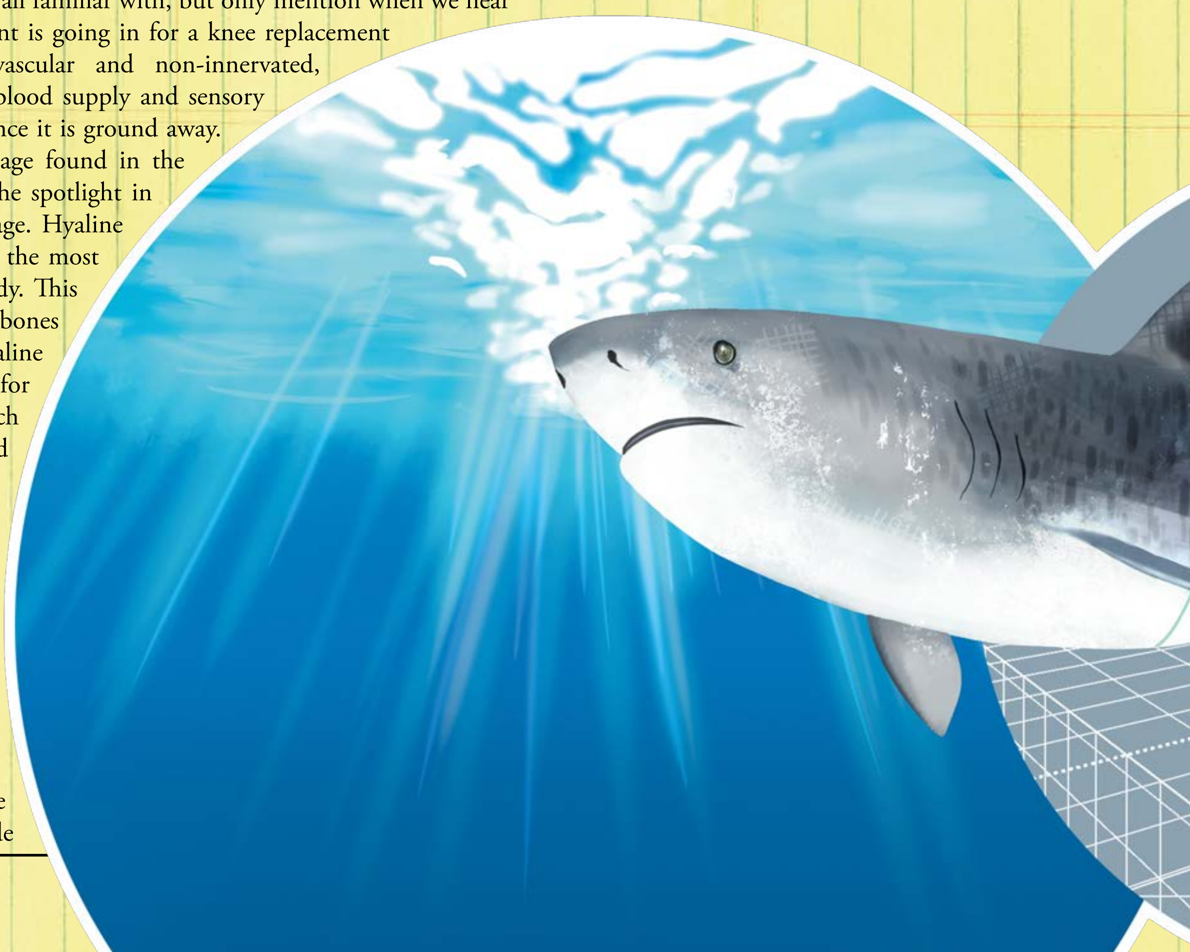
Cartilage. It's a term we are all familiar with, but only mention when we hear that someone's grandparent is going in for a knee replacement surgery. Cartilage is avascular and non-innervated, meaning that without a blood supply and sensory function, it is unable to regenerate once it is ground away. There are three main types of cartilage found in the human body, but the one that has the spotlight in the biomedical field is hyaline cartilage. Hyaline cartilage is a shiny blue color, and is the most abundant type of cartilage in the body. This cartilage is found at the ends of long bones like the humerus, femur, and ribs. Hyaline cartilage provides a smooth surface for tissues and joints to glide against each other and also provides flexibility and impact support. Recently, biomaterial scientists have been researching ways to create new cartilage to help reduce the stress on bones and the number of joint replacement surgeries needed. The solution to these problems might lie in the biomechanics of 3D printing cell-laden hydrogels.



A hydrogel is a web of polymer chains that is composed of 90 percent water. These gels are highly customizable and can be made with either natural polymers (which are made from polysaccharides and proteins) like collagen, gelatin, and fibroin; synthetic polymers; or a hybrid of both. Natural polymer hydrogels have a low immune response, are biodegradable, and have a lower cost, but do not provide a stable long-term solution because the degradation of the material cannot be controlled. Synthetic fibers, however, exhibit highly modifiable biodegradability, biocompatibility, mechanical properties, and biochemical characteristics, due to the ability to tune their chemical structure and molecular composition. However, synthetic fibers can also lack cell recognition sites, which can affect cell communication, adhesion, and growth. By compounding natural and synthetic fibers together, researchers can create a highly modifiable substance that is compatible with the human body. One popular natural biopolymer is chitosan. Chitosan, which is derived from chitin, is the second most abundant biopolymer in nature. It is found in shells, insect cuticles, and even mushroom envelopes. A chitosan solution, when mixed with cells, provides a successful printing and is stable under simulated physiological conditions. Researchers observed that cells printed within chitosan-HA composite hydrogel had high expression levels for early and late stages of bone-forming indicators. During a clinical test, thermosensitive chitosan-pluronic (CP) hydrogels were synthesized by grafting pluronic, a copolymer, onto chitosan. Researchers revisited the composite hydrogels at 12 weeks of implantation and found partial degradation and cartilage/subchondral tissue forming without persistent inflammation. The cartilage showed that the subchondral region contained hypertrophic cartilage and bone-like tissues. This example shows the potential bio-fabricated hydrogels have in the future after continuous study.

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Bio-fabrication is a process of interweaving cellular and noncellular components to mimic the composition and function of the human tissue. This process could be combined with microcarrier technology, which allows for an expansion of cells while they aggregate and allows for a controlled phenotype. Based on their function and desired host, microcarriers can be placed into one of two categories: solid or liquid. Solid microcarriers are used in humans due to their ability to adhere to and expand cells. Liquid microcarriers, meanwhile, have been used in animals, do not need a specific attachment point, and can be implemented without the use of a scaffold, which is a fibrous structure that is seeded with cells and growth factors to help facilitate healing or growth in a specific area.

For cartilage regeneration, growth factors such as TGF-ß (transforming growth factor) are added to help the differentiation of stem cells in the hydrogel. Too much growth factor, however, can lead to excess hypertrophy. These growth factors can be delivered by freeform in a medium, physical blending in the hydrogel, covalent bonding to the hydrogel, microsphere carriers, or by gene delivery. Tissue engineering and clinical treatments still have not been able to create a tissue that is fully functional. Inkjet bioprinting has the potential to mimic the structure of cartilage without causing more damage to the surrounding area. When using thermal inkjet printers, ink droplets are discharged by tiny heated air bubbles at 300˚C for a few microseconds, and the cells are then heated for 2 microseconds, which is 4–10˚C above the normal cell viability level. In a test hydrogel, chondrocytes, which are mature cells that create the matrix of cartilage, were seeded and displayed viabilities of 90 percent. Although chondrocytes show promising results, more research is being done on the long-term growth and possible differentiation into fibroblasts.

Although this is not yet a reality, great strides are being made to repair cartilage defects and regenerate cartilage. Medical grade cartilage may take 10–15 years to become a surgical option, but this is the closest the scientific community has come to creating a vital substance made out of your own body. Stem cells are even more promising for their availability and potential to turn into chondrocytes or osteoblasts. The ultimate goal is to create the best hydrogel; it should have a controlled biodegradability and be able to be regenerated to have a natural structure and perform full cartilage function.