These are examples of types of bone allograft products and purposes they serve. With the chart on page 12, this information can help OR teams determine where a new allograft product would fit into current inventory.

**Allograft cancellous chips**

Cancellous chips, a common nonstructural human allograft bone material, serve as a scaffold for new bone growth. Adding other materials, such as bone marrow aspirate (BMA), provides a scaffold plus the patient’s own cells to stimulate bone growth.

**Synthetics**

Synthetic bone graft materials, such as ceramics, are composed of nonbiologic biocompatible materials such as tricalcium phosphate and hydroxyapatite. They also provide a scaffold, though they are more expensive than biological bone grafts, according to iData Research. Synthetics can be combined with biologics such as BMA.

Vitoss (Orthovita) has the most market share for synthetics at 35%. Vitoss granules are a ceramic material that provides a scaffold into which new bone can grow. Some surgeons add BMA to synthetics to enhance healing capacity.

**Combined products**

Examples of combined products are Vitoss foam and Mozaik (Integra), which include not only ceramics but also bovine collagen, a xenograft. These products provide a matrix for new bone growth and are approved for use with BMA.

**Demineralized bone matrix**

Demineralized bone matrix (DBM) comes in different forms: paste, putty, and strips, among others. This is a large and confusing product group, with dozens of options on the market.

DBMs have both osteoinductive and osteoconductive properties and can be used as graft extenders or enhancers.

Essentially, DBM is allograft bone that has had the minerals removed to expose the bone morphogenic proteins (BMPs) in the bone. The exposed BMPs, particularly BMP-2, are intended to make the allograft osteoinductive, providing signaling factors that induce stem cells to become osteoblasts. Because DBM is a powder, the material is combined with carriers such as sodium hyaluronate, gelatin, or glycerol, that allow it to be molded into a variety of shapes surgeons can more easily use (related article, p 13).
**Bone morphogenic protein**

BMP products, highly concentrated forms of a single bone morphogenic protein produced by recombinant technology, act as osteoinductive agents. These BMPs provide a signal for bone growth that is much more concentrated than those in DBM. The BMPs commercially available today use a bovine collagen carrier, providing an osteoconductive scaffold. The addition of BMA yields a composite that comes close to mimicking autograft.

Two BMP products are on the market: InFuse (Medtronic) and OP-1 (Stryker). InFuse is approved for limited indications, and OP-1 is used under a human device exemption for long-bone nonunions.
A new study in *Spine* documents that between 2003 and 2007, 85% of InFuse used in principal spine procedures was used off-label. The authors note there are still safety concerns with BMP. The FDA issued an alert in 2008 about life-threatening complications when BMP is used off-label in the cervical spine. The Centers for Medicare and Medicaid Services held a meeting in September 2010 to discuss the on-label and off-label uses of BMP.

**Stem cell-based therapy**

A new frontier is allograft products with stem cells. This is the smallest but fastest growing segment of the market, according to Millennium Research Group. These biologics come the closest to replicating autografts because they include the 3 components necessary to form bone:

- mesenchymal stem cells (osteogenic cells)
- cancellous bone matrix (osteoconductive scaffold)
- demineralized bone (osteoinductive factors).

Two stem-cell based products are currently available: Trinity Evolution (MTF/Orthofix) and Osteocel (AlloSource/NuVasive). (At deadline, a new stem-cell product for spine surgery, PureGen by Alphatec Spine, was announced.)

The products are produced using a validated proprietary process in which the immunogenic components of donor bone marrow are removed and the mesenchymal stem cells preserved.

“What remains is the patient’s cancellous matrix that was part of the bone marrow as well as the mesenchymal stem cells and osteoprogenitor cells that were embedded in that matrix,” explains Ray J. Linovitz, MD, FACS, medical director for Orthofix. He notes that as in normal marrow, there are 65-fold more mesenchymal stem cells attached to the cancellous matrix than can be obtained with a bone marrow aspirate.

Demineralized cortical bone from the same donor is added in a consistent ratio to provide additional osteoinductive factors.

Trinity Evolution is regulated by the FDA as an HCT/TP (human cellular tissue/tissue-based product). The main criterion for tissues under this regulation is “minimal manipulation” of cells; that is, the cells are not removed or expanded, and no carriers are added. In contrast, DBM products, which do have carriers, are regulated as medical devices, requiring 510(k) clearance.

Trinity Evolution is labeled for all bone indications. It has been used for spinal fusion and in areas such as foot and ankle surgery for treatment of complex fractures.

**Stem cells: More to come**

Other stem cell products are in the pipeline. They are part of a movement toward tissue engineering, which promises to be exciting and challenging for surgical teams.

“This is sort of a hot topic. Instead of doing fusions or artificial disks, we would like to be able to regrow the disc or at least regenerate cells so they can survive longer,” Dr Linovitz says.

Companies eager to get into the market are marketing cellular products derived from other sources, such as synovial fluid, fat, or amniotic fluid, and seeking to have them regulated as tissue products, he notes. Some are growing stem cells outside the body in quantity and combining them with carriers for indications such as bone growth and cartilage regeneration.
These expanded stem cell products may also be combined with other materials and then are regulated as drugs or devices.

“Surgeons and OR personnel are going to start being inundated by companies saying they have stem cells but from various sources,” he says. “They are going to need to understand the differences in all of these cell sources. We are really at the tip of the iceberg. You are going to see a lot more of this.”

References
Food and Drug Administration. FDA public health notification of complications associated with recombinant human bone morphogenetic protein in cervical spinal fusion. July 1, 2008. www.fda.gov


Rush S. Mesenchymal stem cell allografting in foot and ankle surgery. Foot Ankle Spec. 2010;3(3):140-143, 144-147.