Produced under an educational grant from CeloNova BioSciences, Inc.

Embozene™ Color-Advanced Microspheres

The spherical embolic platform for today and the future.

The technology of safe and reliable embolic agents to occlude the blood supply to tumors and certain arteriovenous malformations and to control bleeding has evolved during the past 35 years. Initially, in the mid-1970s, physicians embolized microvessels with resorbable agents. Practice patterns evolved in the mid-1980s to the use of irregular polyvinyl alcohol (PVA). It was at that time that PVA particles began to be calibrated into defined size ranges. The shift to spherical particles happened because of advances in imaging technology, because the increasing number of pathologies necessitated selectivity of target vessels, and because PVA particles tend to clump and aggregate. This led to the development of well- to super-calibrated spherical embolization devices for predictable vessel occlusion and easy, safe, and targeted delivery.

Although resorbable particles and irregular PVA continue to have their places in embolization, the market is shifting to spherical particles for the treatment of uterine fibroids, hepatocellular carcinoma, liver metastases, preoperative tumors, certain arteriovenous malformations, and bleeding. The only spherical embolic that has been designed from the beginning by physicians and scientists together to provide the user with all of the advantages of spherical particles with added positive design features is Embozene™ Color-Advanced Microspheres, developed by CeloNova BioSciences, Inc. (Newnan, GA). Embozene™ Color-Advanced Microspheres technology is built on four design principles: biocompatibility, precise calibration, suspension, and particle integrity (Figure 1).

BIOCOMPATIBILITY

Spherical embolization particles are devices that are left behind in the human body; it is essential that they do not cause any unnecessary foreign body reaction, inflammation, or local vessel irritation at the points of contact with the body. This is especially important when treating diseases in which additional postprocedural local vessel inflammation is harmful, such as hepatocellular carcinoma.

Embozene™ Microspheres are built of a hydrogel core and coated with CeloNova BioSciences' proprietary polymer, Polyzene®-F, which has unique properties that improve medical devices. Polyzene®-F offers biocompatibility that is near bioneutrality because it does not trigger inflammatory reactions, does not allow platelet adhesion, and is bacterial resistant (among other properties).

CALIBRATION

Because one sphere can occlude one vessel (geometrically, a sphere is the most logical shape to occlude a vessel), the

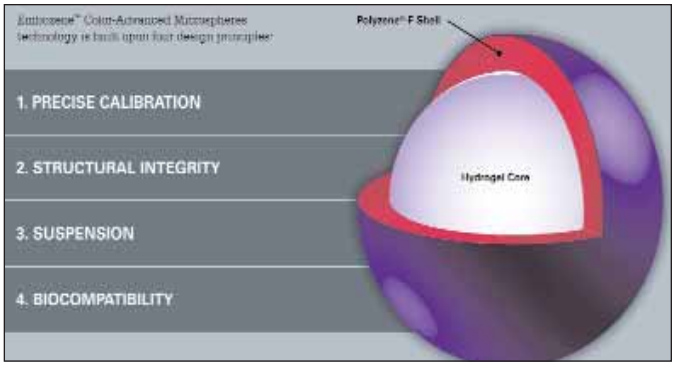

Figure 1. Four design principles of Embozene™ Microspheres.

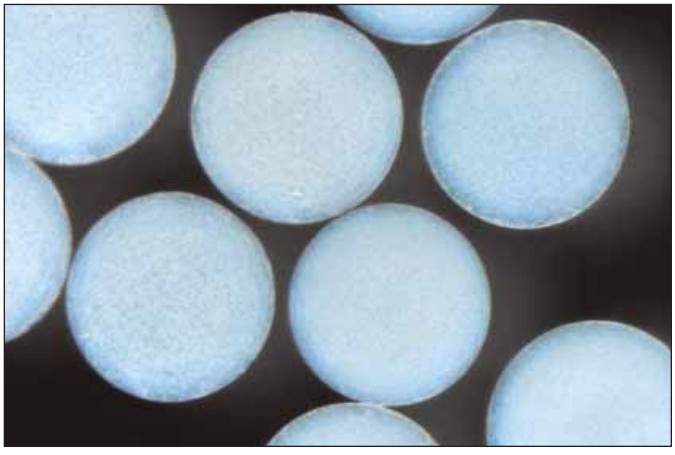

Figure 2. Five hundred-µm Embozene™ Microspheres showing the consistent calibration of size.

calibration of the initial sample that is injected is important for proper targeting. The availability of a variety of precisely calibrated sizes allows for the possibility to upsize during the procedure if dangerous anastomoses with surrounding organs present. This adds control and safety to the procedure.

Embozene™ Microspheres are the most tightly calibrated spherical particles available, with size ranges from ±10 µm for the smallest 40-µm particles, to ±25 µm for the 100-µm particles, to ±50 µm for the 250-, 400-, 500-, and 700-µm sizes, and up to ±75 µm for the largest 900-µm particles (Figure 2). This is in contrast to ranges of several hundred microns for other microspheres, eg, 500 to 700 µm, not including particles outside that size.

Figure 3. Embozene™ Microspheres can maintain their suspension indefinitely.

SUSPENSION

Calibration alone is not sufficient for optimal outcomes. The spheres need to be injected while they are in suspension (Figure 3). This allows for smooth passage through the microcatheters and for each sphere to travel individually to its end destination without aggregation or friction with other spheres. This is essential for proper vessel targeting. Embozene™ Microspheres have the most durable suspension of any embolic particle, with customized mixing recipes per type of contrast used. Each size of sphere requires a specific volume or range allowance of contrast medium to be added to reach full equilibrium with the medium. This customized mixing recipe is also unique to Embozene™ Microspheres because the industry normally recommends an approximate 50/50 mixture of contrast medium to physiological solution.

The outcome is that other spherical embolics get into a temporary suspension that is lost within a couple of minutes, requiring the user to shake the syringe and inject rapidly. Embozene™ Microspheres, once in optimal suspension, remain in equilibrium throughout the procedure, so the operator can take the time required for proper catheter positioning and, when ready to inject, does not need to shake the mixture and inject rapidly. The operator has full control of the injection rate and amount of embolic injected. Given the importance of the endpoint determination in any embolization procedure, this minimizes or eliminates complications that result from untargeted necrosis.

Figure 4. Embozene™ Color-Advanced Microspheres.

Finally, if during injection through the microcatheter the particles fragment or do not rebound, the reason for calibration is lost. What ultimately matters is the size and volume of the particles exiting the microcatheter and flowing into the blood stream and occluding vessels.

PARTICLE INTEGRITY

This is where the fourth principle of the Embozene™ technology comes into play: particle integrity. Embozene™ Microspheres have a shape memory that allows them to compress up to 35% and immediately regain their initial volume upon exiting the microcatheter. Studies have shown that Embozene™ Microspheres not only preserve their initial volume but also do not fragment. This can be tested easily with extreme cases. When the largest Embozene™ spheres (900 µm) are injected through microcatheters with an inner diameter of .021 inches, they immediately regain their initial volume upon exiting without any deformation or fragmentation. Embozene™ Microspheres are the only spherical embolic platform with a 900-µm size that can pass through a microcatheter. Thus, physicians who must upsize to 900-µm particles need not withdraw a microcatheter to replace it with a larger one.

COLOR CODING

To maximize safety and convenience, each sphere was colored according to the industry convention (Figure 4). This helps to eliminate size-selection errors or mistakenly injecting spheres when the intention is to inject other fluids in the event of fluid contamination.

THE PLATFORM FOR THE FUTURE

The outcome of these combined features is a platform that has succeeded in optimizing every parameter relevant to the embolization procedure. Added to the fact that Polyzene®-F is not only an anti-inflammatory surface modifier but also has the ability to elute different hydrophobic, as well as hydrophilic, agents and drugs, it becomes evident why Embozene™ Color-Advanced Microspheres are the embolization platform for today and for the future. ■