Comparative Study of Four Different Spherical Embolic Particles in an Animal Model: A Morphologic and Histologic Evaluation

José I. Bilbao, MD, PhD, Esther de Luis, MD, PhD, José A. García de Jalón, DVD, PhD, Alba de Martino, DVD, María D. Lozano, MD, PhD, Antonio Martínez de la Cuesta, MD, and Bruno Sangro, MD, PhD

PURPOSE: To perform a study in a porcine model comparing four different spherical embolic particles in terms of postembolization patency, deformation, and potential for recanalization, with a focus on a relatively new agent—HepaSphere.

MATERIALS AND METHODS: Partial embolization of both kidneys was performed in 18 pigs. Nine animals were sacrificed at 48 hours and nine at 4 weeks. In the same animal, the right kidney was embolized with HepaSphere particles ("dry" size, 50–100 μm; presumed final size, 200–300 μm), and the left kidney was alternatively embolized with EmboSphere (100–300 μm), Contour (150–350 μm), or Bead Block (150–350 μm) particles. The authors analyzed the size, deformation, and number of particles in each vessel, their morphologic characteristics, and recanalization.

RESULTS: Particle sizes and deformation (1,096 particles) were as follows: HepaSphere, 225.3 μm ± 67 and 26% ± 19.7, respectively; EmboSphere, 132.9 μm ± 36 and 18.1% ± 14.2; Bead Block, 108.1 μm ± 38 and 16.5% ± 13.9; and Contour, 240.8 μm ± 135 and 55.5% ± 33. HepaSphere and Bead Block particles were distally located, and EmboSphere and Contour particles were located more proximally. EmboSphere and Bead Block particles were round, HepaSphere particles were round and/or ovoid, and Contour particles had an amorphous aspect. EmboSphere particles had a higher tendency to aggregate. No recanalization was seen with HepaSphere particles, and variable recanalization was observed with the others.

CONCLUSIONS: Despite similar initial morphologic characteristics, the performance of the agents tested in this study differed in terms of final size, shape, deformation, and luminal recanalization. These differences have potential clinical relevance, and the knowledge of the differing embolic performance may be helpful in choosing agents for specific therapeutic purposes.

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Abbreviations: GMNC = giant multinucleated cell, H-E = hematoxylin-eosin, PVA = polyvinyl alcohol

CALIBRATED spherical microparticles were developed with the aim to avoid the shortcomings of nonspherical polyvinyl alcohol (PVA) particles. Unlike PVA, the former exhibit a homogeneous morphology and have more precisely calibrated diameters, thus decreasing, theoretically, the possibility of too distal embolization (1,2). In addition, aggregation of nonspherical particles can cause the occlusion of large-caliber vessels as well as the obstruction of the catheters used in the procedure (3).

Different types of spherical particles are currently available. Calibrated tris-acrylic gelatin microspheres (EmboSphere; Biosphere Medical, Roissy, France) have been present since 1996 (4). More recently, two spherical PVA particles were developed, Contour SE (Target Therapeutics, Boston Scientific, Fremont California), available since 2000, and Bead Block (Biocompatibles, Farham, UK), available since 2002.

These particles are calibrated in the range of 150–1,000 μm. So calibrated, these agents theoretically permit precise embolization of arteries of any desired vessel. Their clinical usefulness has been demonstrated in a wide variety of clinical situations and in the treatment of uterine myomas (5–8), arteriovenous malformations (9), bone and head and neck tumors (10), and hepatocellular carcinomas (11,12), among others (13).

From the Departments of Radiology (J.I.B., E.d.L., A.M.d.l.C.), Pathology (M.D.L.), and Internal Medicine (Liver Unit)(B.S.), Clínica Universitaria de Navarra, Universidad de Navarra, Avenida de Pio XII, 36, 31008 Pamplona, Spain; and the Department of Histology, School of Veterinary, Universidad de Zaragoza, Zaragoza, Spain (J.A.G.d.J., A.d.M.). Received November 7, 2007; final revision received July 3, 2008; accepted July 14, 2008. **Address correspondence to** J.I.B.; E-mail: jibilbao@unav.es

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Table 1
Technical Aspects of the Embolization Procedure

Animal	Time of Sacrifice	Right Kidney Material	Amount (mL)	Embolization Time	Left Kidney Material	Amount (mL)	Embolization Time
1	48 h	HepaSphere	1.5	2 min	Embosphere	4	2 min15 sec
2	48 h	HepaSphere	1.5	2 min	Embosphere	5	2 min
3	48 h	HepaSphere	2	1 min	Embosphere	5.5	2 min
4	48 h	HepaSphere	1	2 min	Bead Block	4	1 min
5	48 h	HepaSphere	2	2 min 30 sec	Bead Block	4	2 min
6	48 h	HepaSphere	1	30 sec	Bead Block	3	1 min
7	48 h	HepaSphere	1	1 min	Contour	6	2 min
8	48 h	HepaSphere	1.5	30 sec	Contour	8	1 min 30 sec
9	48 h	HepaSphere	1	1 min	Contour	6	2 min 30 sec
10	4 wk	HepaSphere	2	2 min	Embosphere	4	1 min
11	4 wk	HepaSphere	1	1 min	Embosphere	6	2 min
12	4 wk	HepaSphere	1.5	1 min	Embosphere	5	2 min
13	4 wk	HepaSphere	1	1min	Bead Block	5	3 min
14	4 wk	HepaSphere	2	2 min	Bead Block	5.5	2 min
15	4 wk	HepaSphere	1	2 min	Bead Block	3.5	1 min
16	4 wk	HepaSphere	1	1 min	Contour	6	2 min
17	4 wk	HepaSphere	2.5	1 min 30 sec	Contour	9	2 min 30 sec
18	4 wk	HepaSphere	2	2 min	Contour	7.5	2 min

HepaSphere is a new spherical embolic particle developed in 1996 by Hori et al in Japan (14). Initially referred to as superabsorbent polymer microspheres, they are nondegradable and nontoxic. HepaSphere is a copolymer of sodium acrylate and vinyl alcohol, which has been used in Japan for the treatment of hepatocellular carcinoma, and histologic studies have demonstrated the complete occlusion of the intratumor vessels without necrosis of the healthy liver tissue (12). HepaSphere has also been used as embolic material in the percutaneous treatment of arteriovenous malformations (9).

This new particle is calibrated in range of 50 μm and possesses a characteristic that distinguishes it from the rest of calibrated spherical particles in that it is developed in a dry state (powder form). Experimental studies performed with HepaSphere particles in animal models have demonstrated that there are no differences in terms of in vivo size depending on the contrast media used for the dilution (ionic and nonionic) and that particles of 50 μm in the dry state will enlarge to a size of 200–300 μm (15).

The aim of this study was to evaluate the performance of HepaSphere particles and the other three calibrated spherical particles. The information could be of relevance, and have clinical usefulness, when selecting the most adequate particle for a specific purpose.

The objectives of this experimental study were, first, to compare the differences in the particles in terms of final location, shape, and deformation and to study, histologically, the patency and possible recanalization of the occluded arteries.

MATERIALS AND METHODS

The experiment was conducted after the approval of the ethical committee of our University. Eighteen female pigs (Large white *suis scrofa)* weighing 25–28 kg were included in the study. The common pig is a good animal model for the study of embolization because its vascular anatomy is similar to that of humans and its mean size and body weight (30 kg) allows extrapolation of the results to clinical practice. Moreover, embolization can be carried out by using the same materials (catheters, introducers) employed in humans. The pig also has a fibrinolytic system very similar to that found in humans (16). The kidney model has been used by some authors to study embolizing materials because it is a double organ, which, therefore, allows comparative studies, and the diameters of the embolized arteries may be predicted in advance (15).

To know the acute effect of the particles as well as the mid-term results after evaluation, nine animals were sacrificed 48 hours after embolization. The remaining nine animals were sacrificed 4 weeks after the procedure.

In this study, four different particles were used, diluted with iodixanol (Visipaque 270; Amersham Health, Oslo, Norway). HepaSphere particles, the first material used, are calibrated microspheres composed of sodium acrylate and vinyl alcohol copolymer (Biosphere Medical). In the dry state, the particles are 50–100 μm in diameter. As said before, this material was chosen because their end size after reconstitution with contrast medium is approximately 200–300 μm (9,12). The second material used, EmboSphere particles, is composed of calibrated microspheres made of tris-acrylic gelatin (Biosphere Medical). They measure 100–300 μm in diameter. The third material, Contour calibrated microspheres, is composed of PVA (CSE, Target Therapeutics, Boston Scientific) and measure 150–350 μm in diameter. Bead Block calibrated microspheres, the fourth material used, are composed of PVA (Biocompatibles) and are 150–350 μm in diameter.

These sizes were selected in an attempt to ensure the maximum possible similarity among the different materials. Embolization was carried out as shown in **Table 1**. The right kidney was always embolized with HepaSphere particles, whereas the left kid-