INTRODUCTION
A traditional and effective approach to categorizing spherical embolic agents relates to their tendency to cause a permanent or temporary vascular occlusion. However, it is also becoming important to define whether the embolic agent itself is temporary or permanent. The most commonly used microspheres, including Triacryl gelatin, polyvinyl alcohol and polyphosphazene-coated PMMA microspheres, are all permanent agents which remain in the body indefinitely after they are administered. This is not dependent on whether or not the treated vessel recanalizes with time.

There is an inherent appeal to the concept of resorbable microspheres. All embolization procedures are performed for certain indications, and if the goal of the procedure can be accomplished without implanting a permanent foreign body into the patient, then that should be further explored and potentially preferred. In 2007, Laurent et al (1) defined a set of four characteristics in an ideal resorbable microsphere would demonstrate:

• A controlled resorption time not influenced by enzymatic potential.
• A limited local inflammatory response
• A return of complete functionality of the target bed after embolization
• Ease of drug loading

If an agent can meet these criteria, it would ensure that the target pathology could be effectively treated while also allowing the target organ to fully recover. Presently, several resorbable microspheres are in various stages of development.

STARCH-BASED MICROSPHERES
Degradable starch microspheres have been used for several years and are available under the trade name Embocapt® S (Pharmacope; Berlin, Germany) (Figure 1). These spheres have been utilized for liver-directed tumor therapy (3,4). A drawback associated with these spheres is that they have an average diameter of 50 microns and a range of 20-200 microns. The microspheres are degraded by serum alpha-amylase, resulting in a short half-life of 35 minutes. This limits their utility for many applications requiring particulate embolization.

The pathologic changes seen after embolization with Embocapt® S have been studied in a swine model (5). In this study, embolization of the hepatic arteries was performed with these starch microspheres. Angiograms were performed until vessel recanalization was detected, which occurred on average of 32 minutes (range 26-39 minutes). Three hours after recanalization was observed, the animals were sacrificed. Pathologic evaluation demonstrated no signs of tissue hypoperfusion or tissue necrosis. In fact, no differences were found between untreated and embolized tissue (5). The normal hepatic architecture was preserved after embolization. Only rare particles were seen within the sinusoids. While the short half-life limits their utility for many applications requiring particulate embolization, this animal study demonstrated that if the half-life can be extended, then these microspheres can accomplish that while preserving normal hepatic architecture. For example, it has been suggested that the administration of degradable starch microspheres prior to chemoembolization (6) or radioembolization (7) can potentially protect the tumor-free liver tissue from the effects of these procedures.

CARBOXYMETHYLCELLULOSE & CHITOSAN-BASED MICROSPHERES
Weng et al have done work with biosorbable microspheres prepared from carboxymethylcellulose and chitosan (N-acetylgalactosamine), which is a linear polysaccharide derived from chitin after deacetylation (Figure 2). Carboxymethyl chitosan can then be cross-linked with oxidized carboxymethylcellulose to form microspheres through an inverse emulsion method. The preparation method, and specifically the degree of cross-link density, appears to directly correlate to the resorption time. The cross-link density also appears to have an inverse relationship with compressibility. Therefore, a microsphere with more densely packed crosslinks will be less compressible and lead to a more proximal vascular occlusion than microspheres of equal diameter with a lower crosslink density. The spheres do not aggregate due to a low coefficient of surface friction. The carbonyl groups in the microsphere matrix in addition to the carboxylic groups in the microsphere matrix in addition to the carboxylic groups in the microsphere matrix in addition to the carboxylic acids. These microspheres are available for use today and have been their utility for many applications requiring particulate embolization, hepatic architecture was preserved after embolization. Only rare hours after recanalization was observed, the animals were sacrificed which occurred at a mean of 32 minutes (range 26-39 minutes). Three

PLGA-BASED MICROSPHERES
Polyactic-glycolic acid microspheres coated with type I bovine collagen have been evaluated as a resorbable embolic (Figure 3). These microspheres are amorphous and create a vascular occlusion both mechanically and by binding platelets. The published evaluation of these microspheres took place in a sheep model (17). In this study, an in vivo comparison of UAE was performed between 150-212 micron PLGA microspheres and 300-500 micron trisacryl gelatin microspheres. There was no difference in the time to occlusion and in the amount of embolic required for embolization. However, it is important to remember that every embolization procedure is performed in order to accomplish a pre-defined clinical goal. If that goal can be accomplished without implanting a foreign body then it becomes difficult to rationalize the use of a permanent embolic implant. It is worth repeating that clinical efficacy must be convincingly demonstrated before this change of thought can be supported. In addition, the cost of any price premium for a resorbable agent must be justified. If those two points can be addressed, then it is likely that many interventionalists and even more patients will opt for resorbable agents for their embolization procedures.

GELATIN-BASED MICROSPHERES
Gel-Base Microspheres (Vascular Solutions, Inc) are made from purified skin gelatin, which contains Gluteraldehyde bridges between amino acids. These microspheres are available for use today and have been successfully used clinically. Preclinical studies have shown that these microspheres degrade within 12 weeks. However, degradation was not always accompanied by recanalization. While used today for particulate embolization, it does not appear that they meet the ideal criteria for a resorbable agent given the fact that the potential for recanalization may be limited by the associated inflammatory reaction, despite the degradation of the microspheres.

CONCLUSIONS
Resorbable microspheres represent the next frontier in particulate embolic technology. The benefits of resorbable technology, assuming equivalent clinical efficacy to existing embolic agents, are readily apparent when comparing it with uterine fibroids, tumors (both benign and malignant) in various locations, and other clinical conditions. The potential for recanalization and restoration of native blood flow can have implications on organ function, treatment capabilities, and the avoidance of potential long-term yet unknown risks of permanent embolic agents. With time, it has become clear that permanent embolic agents do not carry significant long-term risk when used for embolization for a number of different clinical indications. However, it is important to remember that every embolization procedure is performed in order to accomplish a pre-defined clinical goal. If that goal can be accomplished without implanting a foreign body then it becomes difficult to rationalize the use of a permanent embolic implant. It is worth repeating that clinical efficacy must be convincingly demonstrated before this change of thought can be supported. In addition, the cost of any price premium for a resorbable agent must be justified. If those two points can be addressed, then it is likely that many interventionalists and even more patients will opt for resorbable agents for their embolization procedures.

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RESORBABLE MICROSPHERES: THE NEXT FRONTIER IN EMBOLIC TECHNOLOGY

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