Biodegradable Materials Available for Transarterial Embolization

Tushar Garg, MD [1]*, Adham Khalil, MD [1], Prateek Gowda, BS [1], Anna Gong, BA [1], Robert Weinstein, BE [1], Clifford R. Weiss, MD, FSIR, FCIRSE[1]

[1] Division of Vascular and Interventional Radiology, The Russell H. Morgan Department of Radiology and Radiological Science, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Learning Objectives

To review all available novel biodegradable occlusion technologies for vascular embolization and compare their properties and preclinical data to provide a reference for interventional radiologists interested in this field.

Background

Over the last decade, there has been increased interest in the development of biodegradable embolic agents for transarterial embolization (TAE) procedures. The goal of degradable embolic agents is to provide effective embolization on a transient basis. These embolic agents are removed from the body after achieving the intended clinical outcome without interfering with the function of other organs. Removing these agents will potentially minimize long-term sequelae of permanent embolic agents like alternations in histological architecture, vascular capacitance, and injury to tissue due to “on” or “off” target deposition.

Ideal Biodegradable Material

An ideal biodegradable embolic should have predictable and effective target occlusion along with 1) tailored degradation timeframes to provide adequate infarction of the target tissues in a large number of indications with subsequent return of flow, 2) a variety of tightly calibrated particle size distributions to allow optimization of particle delivery according to the anatomy of the target vessel, 3) easily suspendable in physiological solutions, 4) easy delivery through traditional microcatheters, 5) full biological compatibility to minimize safety concerns, and 6) multi-modal imageability to allow for standardization of embolization end points.

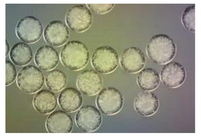
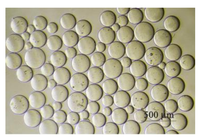
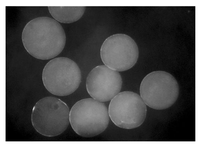
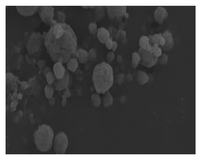
Conclusion

The materials available for embolization have evolved rapidly in the last few decades from autologous blood clots, and muscle tissues to microspheres and gels made up of complex polymers that can be modified for a wide array of functions. The clinical application and development of new agents will continue to expand as the field of endovascular intervention grows.

@gargtushark
@DrCliffWeiss

References

Currently Available Biodegradable Embolic Materials

Biodegradable Materials	Chemistry	Mechanism of Degradation	Advantages	Limitations	Pre-clinical Study Assessing the Particle
Poly[lactic (PLA)-co-glycolic (GLA)] acid 	Hydrophobic linear co-polymer synthesized with different ratios of lactic and glycolic acids. The monomers are linked with an ester bond. The ratio of PLA and PGA is a key component for deciding the degradation rates.	The polymer degrades *in vivo* by hydrolysis of ester bonds between PLA and PGA. PLA undergoes further hydrolysis to form lactic acid which is excreted through cellular activity. PGA undergoes same degradation process and is then excreted by kidneys.	1) Approved by FDA for treatment of unresectable/ inoperable hyper vascularized tumor. 2) Available in multiple particle sizes 3) Full biological compatibility demonstrated and easily suspendable in contrast media 4) No risk of migration due to the biological occlusion	1) Lacks tailored timeframes 2) Lacks multi-modality imageability	**Studied by Owen et al in an uterine artery sheep model** 1) 150-212 µm PGLA particles were used to catheterize and embolize the uterine artery. 2) Time to achieve stasis was comparable to embosphere and found to be suspendable in saline and contrast media 3) Complete degradation seen at 6 months with no residual material 4) Recanalization seen ¾ treated animals at 12 months 5) Embolization effectiveness found to be similar to embosphere up to 6 months 6) No complications seen
PLGA-Polyethylene Glycol (PEG)-PLGA	It has PLGA polymers attached with PEG polymers which are composed of ethylene oxide ranging from 4 to >400.	Degradation starts with hydrolysis of PLGA crosslinks yielding PLGA and PEG. PEG usually does not degrade further and is excrete via the urine.	1) Rapid degradation timeframe limits necrosis 2) Available in multiple particle sizes 3) Easy of delivery	1) Lack of tailored timeframes 2) Toxicity can be seen if PEG degrades 3) Lacks multi-modality imageability	**Studied by Maeda et al in porcine kidney model** 1) 300-500, 500-700, 700-900 µm particles were used 2) Complete degradation at 7 days 3) Complete recanalization seen at 7 days in 700-900 µm particles and partial in 300-500 and 500-700 µm particles
Carboxymethylcellulose (CMC)-chitosan (CMC-CCN) 	CMC polymers are created by varying degradation times by altering the degree of oxidation of CMC. CMC and chitosan are combined in a water-in-oil emulsion to for cross linked polymers.	The CMC-CCN polymer is degraded by lysozyme which is abundant in the human body. It cleaves the Schiff base. Both CMC and chitosan are non-toxic and are excreted by kidneys.	1) Offers range of tailorable degradation timeframes 2) Available in particle sizes from 100 to 1550 µm 3) Easy of delivery	1) Information regarding recanalization and degradation lacking 2) Toxicity concerns due to their size 3) Lack multi-modal imaging	**Studied by Weng et al in rabbit renal artery model** 1) 100-300 µm particles used to embolize renal artery 2) Time to achieve stasis comparable to tris-acryl gelatin 3) Embolization effectiveness found to be similar to tris-acryl gelatin
Chitosan 	Chitosan is a N-deacetylated derivative of chitin and contains multiple free amino acids with a degree of deacetylation >0.65.	It is degraded *in vivo* by lysozyme and the end product is glucosamine. This is used in the body to make glycosaminoglycans, proteoglycans and glycolipids.	1) Easy delivery through microcatheters 2) Low risk of local and systemic toxicity 3) Extended degradation timeframe reduces risk of migration	1) Lack of tailored timeframes 2) Lack multi-modal imaging 3) Different particle size ranges not available	**Studied by Kwak et al in rabbit renal artery model** 1) 150–250 µm particles used to embolize renal artery 2) Not easily injected through the catheter without blockage 3) Shape of particles maintained until 8 weeks, absorption seen at 24 weeks and completed at 32 weeks 4) Embolization effectiveness found to be better than PVA
Hydroxyethyl acrylate (HEA) 	Hydrolytically degradable material synthesized to contain 2 degradation sites using N,N′-(dimethacryloyloxy)adipamide crosslinker (C6NCL) to modulate the rate of degradation.	Degradation occurs in basic conditions and the degradation of hydroxylamines is substituted into the material and linear carboxylic acid. Degradation product can be toxic in large amount.	1) Produces lower rate of ischemia compared to other controls	1) Lack of tailored timeframes 2) Lacks multi-modality imageability 3) Putrescine can be toxic in large amounts 4) No information on different sizes	**Studied by Schwarz et al in renal artery canine model** 1) 300–500 µm particles used to embolize renal artery 2) Occlusion lasted for 10-14 days (critical period) 3) Recanalization seen at 3 weeks 4) Embolization effectiveness found to be similar to EmboGold up to 2 weeks 5) No complications seen