GPX by Fluidx Medical: A New Biomimetic in situ Setting Embolization Agent

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Disclosure

Speaker name: Jihad A. Mustapha

I have the following potential conflicts of interest to report:

Consulting: Abbott Vascular, Bard Peripheral Vascular, Boston Scientific, Cagent Vascular, Cardiovascular Systems, Inc., Cook Medical, Medtronic, PQ Bypass, Spectranetics, Terumo Medical
Over 4 million coils, particles, and liquid embolics are used each year for peripheral and neuro embolization procedures to embolize tumors, seal aneurysms, close leaks in aneurysm grafts, seal arterial venous malformations (AVMs), stop bleeding, and other like uses.
EMBOLICS: Used Throughout the Body

Intracranial
- Aneurysms, AVM’s, bleeds

Head & Neck
- Epistaxis, carotid blowout syndrome

Thoracic
- Hemoptysis, Aneurysms, Pulmonary AVM

AAA / TAA Endoleaks
- Coils and/or Liquid embolics (high volume)

Upper & Lower GI Bleeds
- Coils, Gelfoam, Microparticles

Peripheral / Visceral
- AVM’s, aneurysms, dialysis AVF’s

Tumors
- (multiple sites / organs)
- Microspheres +/− Chemotherapy (TACE) Radioembolization

Gynecologic
- Uterine fibroids, artery, pelvic congestion

Vessel Trauma
- (multiple-solid organ, limbs)
- Coils, Gelfoam (pelvis), Covered stents

Genitourinary (BPH)
- Particles, Microspheres, Gelfoam (rare), Coils

Varicose Veins
- Laser therapy, Ablation, Sclerotherapy
**PROBLEM:** Control, Inconsistency, Delivery

- **Particulates** are widely used but are associated with delivery errors including unintended proximal reflux, catheter clogging, and clumping.

- **Coils** are widely used but associated with migration in high-flow environments, inconsistent embolization requiring multiple coils, and high-cost.

- **Liquid embolics** have some advantages in distal & small vessel embolization, but are cytotoxic, difficult to control, and associated with numerous catheter delivery issues, patient injuries, FDA warnings, and high cost.
The tentacles of the sandcastle worm select individual grains of sand then secrete tiny dabs of liquid “glue” on the grain then places it on the tube structure. The tentacles adjust the location of the grain of sand. Full solidification occurs within 25 seconds and worm proceeds with next grain of sand.
SOLUTION: GPX Embolic

- Based on marine sandcastle worm tube formation
- A new multi-use embolic designed to improve effectiveness, safety, and delivery
- Combines the benefits of coils, particles and liquid embolics
- Proprietary gel-coated particle (in high salinity)
- A phased electrostatic transition occurs at physiologic salinity
- Non-cytotoxic, Non-hemolytic, Non-inflammatory
- Non-adhesive
- Does not polymerize, does not precipitate
- Ease of control
- Predictable deployment
- Ability to create multiple viscosities
- Compatible with standard catheters
  - Special catheter technology not required
HOW IT WORKS

• Oppositely charged components are attracted to each other

Production Phase  Pre-Filled Syringe  Ionic Gel – Embolic State
HOW IT WORKS

- Oppositely charged components are attracted to each other
- Highly concentrated NaCl acts as a barrier to the electrostatic attraction
- Reduced NaCl concentration induces solidification
- Human blood is ~150mM NaCl
  - Relatively low NaCl concentration
  - In this environment, GPX solidifies
  - During microcatheter delivery, NaCl concentration is ~1600 mM, enabling ease of delivery and maximizing control
  - Upon exiting the catheter, the NaCl concentration drops from 1600mM (packaging) to 150mM (human blood)
  - GPX solidifies in moments at the capillary (~10um) level of occlusion
- Range of different viscosities possible
- Non-polymerization / non-precipitation
GPX - SOLIDIFICATION

GPX injected underwater
• Immediate solidification
• Syringe easily removed
• Aggressive shaking
• No break up of GPX

GPX Viscosity
• In syringe: Approx 1000 cps
  • Similar to Castor Oil
• After Solidification: Approx 30,000,000 cps
  • Similar to Pliable wax (i.e., wax ear plug)
TECHNOLOGY

- GPX Bench Tests
- Successful acute in-vivo studies
- Successful chronic in-vivo studies
- Passed cytotoxicity and hemolysis tests
- Does not “glue” catheters in place
- Allows for improved control in delivery
TECHNOLOGY – GPX with Coil

BSC VortX 18 Coil in 4.7mm ID Tubing...Flow is not stopped at 120mmHG

~0.10ml GPX 35 Particle Embolic proximal to BSC VortX 18 Coil...Proximal pressure 120mmHG, distal flow immediately arrested to drip

Distal air bubble
GPX - Injectability

GPX is formulated for use in standard microcatheters

In a 0.026” (0.66 mm) ID catheter (135 cm), injection pressures are 1.4 Mpa, well below rated catheter limits at 0.3 mL/min
GPX: Pre-Mixed/Pre-Filled Syringe

- Particles ➔ Liquid ➔ Gel ➔ Solid
- GPX is pre-mixed as part of manufacturing process
- No Polymerization / No Precipitation
- Produced in a single syringe, ready to inject
- Works with standard microcatheter

Fluidx GPX injected through 135cm microcather (BSC Renegade 0.027” 2.8F)
Quantifying Solidification

<table>
<thead>
<tr>
<th>Coacervate</th>
<th>Complex Modulus (G*) kPa</th>
<th>Storage Modulus (G’) kPa</th>
</tr>
</thead>
<tbody>
<tr>
<td>GPX after 24 hours in BSS</td>
<td>195 (+/- 36.2)</td>
<td>123 (+/- 27.9)</td>
</tr>
<tr>
<td>PG-MP +Ta 1400 mM</td>
<td>0.025 (+/- 0.009)</td>
<td>0.006 (+/- 0.005)</td>
</tr>
</tbody>
</table>

*1 Hz, 1% Strain
GPX – No Catheter Adhesion

Force to remove catheter from GPX measured at 2 minutes and 24 hours after injection into saline (BSS).
GPX – No Catheter Adhesion
GPX injected deep into rabbit kidney vasculature. No signs of systemic adverse effects were observed during or after injection.

GPX in-vivo injected proximal & distal to catheter...catheter easily removed after 2-minutes post injection.
GPX – Animal Study

GPX injection into small animal (rabbit) ear

Note distal flow of embolic

GPX post-injection
Full filling of vasculature

GPX 5-6 min post-injection
GPX – Large Animal Study

- Good distal penetration into fine blood vessels
- Created stable, controllable occlusions
- Microcatheter easily withdrawn multiple times from 1-2cm of embolic that had refluxed around the tip
  - No evidence of any “gluing” effect of catheter onto blood vessel sidewall
  - Microcatheter used to “pack” material with minimal adhesion

Pre-Embolization

Post-Embolization
COMPLETE ARTERIAL OCCLUSION...NO VENOUS MIGRATION
Non-Hemolytic

- Hemolysis testing was done in commercial laboratory and method satisfies ISO-10993-4 standards
- ASTM Direct Contact Method
- Material was non-hemolytic
- Score: 0.08
  - Well within non-hemolytic range (0-2.0)
Non-Cytotoxic

- Testing was done in commercial laboratory and method satisfies ISO-10993-5 standards
- MEM Elution Method
- Reactivity: None (0)
- Score: Pass (0-2 is passing range)
<table>
<thead>
<tr>
<th>Embolic Type</th>
<th>Clinical Use</th>
<th>Limitations/Concerns</th>
<th>GPX Advantages</th>
</tr>
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<tbody>
<tr>
<td>Particulate Embolics: Spheres</td>
<td>Tumor devascularization</td>
<td>Arterial use only</td>
<td>Arterial and venous use</td>
</tr>
<tr>
<td>and Particles</td>
<td>Pre-surgical hemostasis</td>
<td>Non-target embolization possible via shunts and reflux</td>
<td>Non-migrating</td>
</tr>
<tr>
<td></td>
<td>Targeted delivery of chemotherapy</td>
<td></td>
<td>Predictable deployment</td>
</tr>
<tr>
<td>Coils</td>
<td>Aneurysms</td>
<td>Unit and procedure cost</td>
<td>Lower procedure cost</td>
</tr>
<tr>
<td></td>
<td>Arteriovenous malformation</td>
<td>Specific catheters required</td>
<td>Standard catheters can be used</td>
</tr>
<tr>
<td></td>
<td>Shunts</td>
<td>Unpredictable deployment</td>
<td>Predictable behavior maximizes physician control</td>
</tr>
<tr>
<td></td>
<td>Revision of endoprosthesis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polymerizing /Precipitating</td>
<td>Aneurysms</td>
<td>“Finicky” prep and control of embolic</td>
<td>Pre-mixed</td>
</tr>
<tr>
<td>Embolics</td>
<td>Arteriovenous malformations</td>
<td>Catheter entrapment</td>
<td>Formula maximizes control and deployment in challenging anatomy</td>
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Proprietary Gel-Coated Particle
- Injectable / Flowable Particle
- Improved Delivery
- No prep – Pre-Filled syringe “Ready-to-use”
- Precise and Predictable Control
- No Polymerization and No Precipitation
- Non-Cytotoxic, Non-Hemolytic, and Non-Inflammatory
- Will Not “Glue” a Catheter in Place
- Multiple viscosities available
- GPX may represent a promising new embolic agent for a variety of embolization scenarios
Thank You

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