Absorbable Hydrodissection Gel

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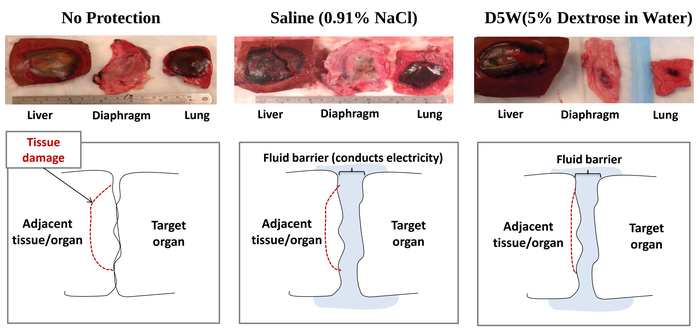
Introduction

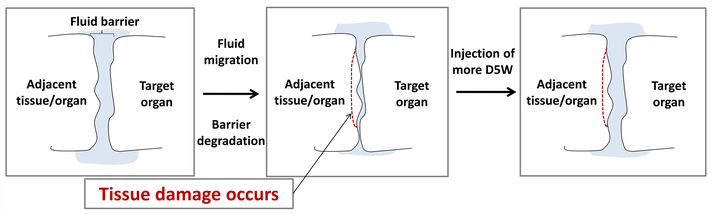
Radiofrequency (RF) ablation and cryoablation are two techniques used to treat some of the 500,000 new cases of hepatic cancer every year [1]. Recently, great strides have been made in improving the efficacy, safety, and cost of these minimally invasive procedures [2].

Imaging of the treatment area is commonly provided by ultrasound or CT scans. The ablation probe is inserted into the treatment site. Eradication of the tumor results from tissue necrosis due to extreme temperatures [3]. To protect adjacent tissue, hydrodissection is performed.

Hydrodissection is a procedure where a fluid is injected between two tissue layers to create a barrier. For ablation procedures, common hydrodissection fluids are CO_2, saline, and 5% dextrose in water (D5W) [4]. The problems current technologies pose are fluid migration within the peritoneal cavity and subsequent barrier degradation [5]. To prevent this, a thermoreversible poloxamer solution was developed.



The problem with D5W (5% Dextrose in water)



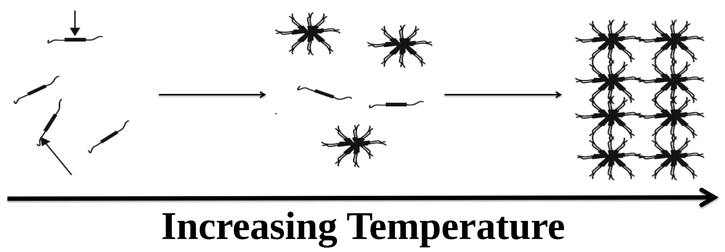
Design Specifications

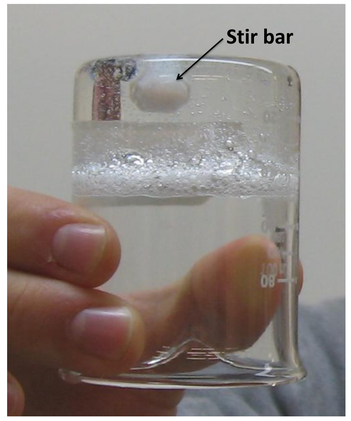
- *Biocompatibility* - Product must be completely biodegradable or bioabsorbable, and non-allergenic.
- *Electrical/Thermal Insulator* - Product must provide adequate protection to surrounding tissue.
- *Viscosity* - Product must prevent fluid migration and barrier degradation.
- *Ergonomics* - Product must not significantly alter current hydrodissection techniques.
- *Cost of Materials* - For competitive product marketing, the product must be ≤ $200.

Saline	**Pro**	• Thermal Insulator • Biocompatible
	Con	• Electrical Conductor • Fluid migration • Barrier degradation
D5W	**Pro**	• Electrical Insulator • Thermal Insulator • Biocompatible
	Con	• Fluid migration • Barrier degradation
Ideal Hydrodissection Fluid	**Additional Requirements**	• Increased Viscosity • Decreased fluid migration • Decreased barrier degradation

Design – Poloxamer Thermoreversible Solution/Gel

- *Thermoreversible* - A poloxamer solution would be able to be injected as a fluid which would then form a viscoelastic gel in vivo [6-8].
- *Bioabsorbable* – Poloxamer 407 would be absorbed by the body, processed through the kidneys (MW <13 kDa), and excreted through the urine [6-7].
- *Non-ionic* - Poloxamer 407 is expected to be an electrical insulator similar to D5W [9].
- *Rapid Erosion* – The product is expected to be cleared from the body cavity in 48-72 hours [6].
- *Low mechanical strength* – This is expected to have no effect on the product efficacy since the patient it relatively immobile during ablation procedures [6].

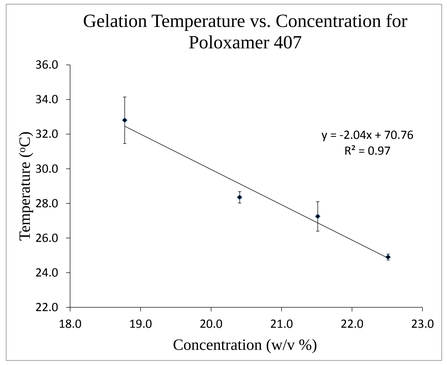




Left: The micellization of poloxamer units as temperature increases. Above: Gelled 21.0% poloxamer during gelation temperature testing.

Testing

Gelation Temperature



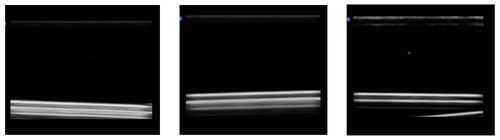
A 19.0% poloxamer solution will gel at 32.0°C.

Imaging

CT Scan

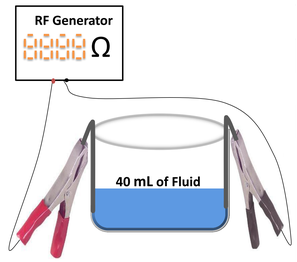
	D5W	19.0% Poloxamer	Gel – 19.0% Poloxamer
ROI	8.9 ± 2.9	14.1 ± 2.5	14.7 ± 2.2
ROI w/ Iohexal	220.6 ± 4.3	106.4 ± 2.3	N/A

Ultrasound



D5W | Poloxamer Solution | Poloxamer Gelled

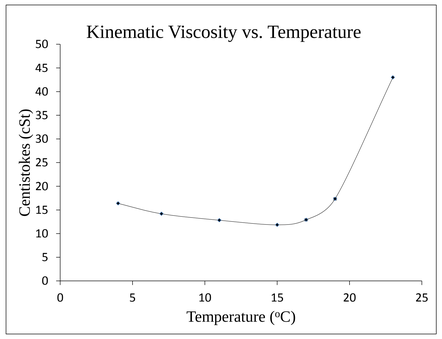
Impedance



Sample	Impedance (Ω)
Blank	40
Saline	88
D5W	High (>1000)
19.0% Poloxamer (solution)	High (>1000)
19.0% Poloxamer (gelled)	High (>1000)

19.0% poloxamer, both in solution and gelled, has comparable impedance with D5W.

Viscosity



19.0% poloxamer was found to have a minimum viscosity at approximately 15°C.

Conclusion

- A 19.0 % (w/v) poloxamer 407 solution will gel at 32°C.
- Poloxamer, both in solution and gelled, will not inhibit imaging (i.e. CT scan, ultrasound) during ablation procedures.
- A 19.0% poloxamer solution will act as an adequate electrical insulator to protect tissue during RF ablation procedures.
- A 19.0 % poloxamer solution can be injected into the body cavity at ~15°C.
- 19.0% poloxamer should suffice as a hydrodissection fluid/gel with similar characteristics to current hydrodissection fluids (i.e. D5W, saline) while preventing fluid migration and barrier degradation.

Future Work

- WARF Disclosure/Patenting
- 'Ease of Injection' testing
- Animal testing
- Toxicity testing
- FDA approval
- Clinical trials
- Additives
  - Poloxamer 188; increase bioadhesion
  - Poly(ethylene glycol) – PEG; decrease fluid viscosity

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Images
Tissues – From [5]
Poloxamer micellization – From [7]