Absorbable Hydrodissection Fluid

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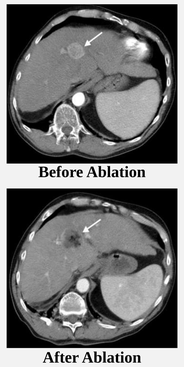
Introduction

Radiofrequency (RF) and cryo-ablation are two techniques used to treat some of the 500,000 new hepatic cancer cases every year [1]. Great strides are being made in improving the efficacy, safety, and decreasing the cost of these minimally invasive procedures.

Imaging of the treatment area is commonly provided by ultrasound or CT scan. The ablation probe is inserted within the tumor tissue and extreme temperatures cause necrosis [2]. To protect healthy tissues, a fluid barrier (resulting from hydrodissection) is established between tissues. Common hydrodissection fluids include saline and 5% dextrose in water (D5W) [3]. Due to the low viscosity of these fluids and the pressure within the peritoneal cavity, fluid migration and subsequent barrier degradation occur during the ablation procedure [4]. To prevent this, a poloxamer solution was developed which forms a viscoelastic gel after injection between the tumor and healthy tissues.

Hepatic tumor ablation

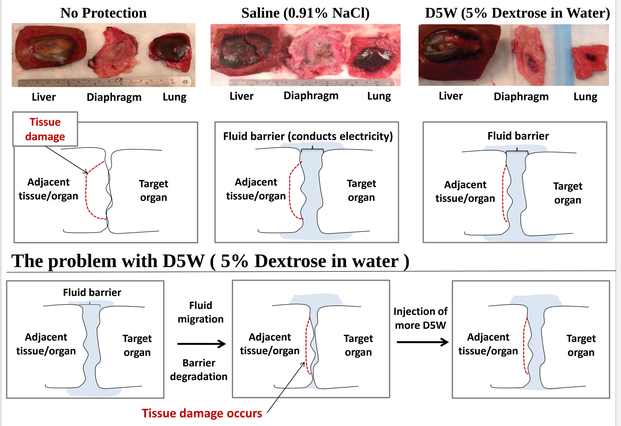
(White arrow points to tumor)



Before Ablation

After Ablation

Protection provided by currently used hydrodissection fluids



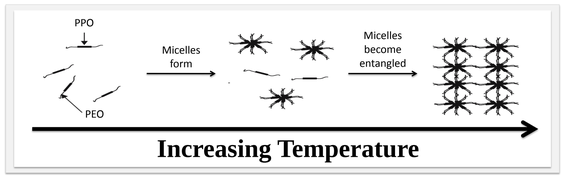
The problem with D5W (5% Dextrose in water)

Design Specifications

- ***Biocompatibility*** **- Materials must be completely biodegradable or bioabsorbable, and non-allergenic.**
- ***Electrical/Thermal Insulator*** **– Design must provide adequate protection to surrounding tissue.**
- ***Viscosity*** **- Design 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 ≤ $250.**

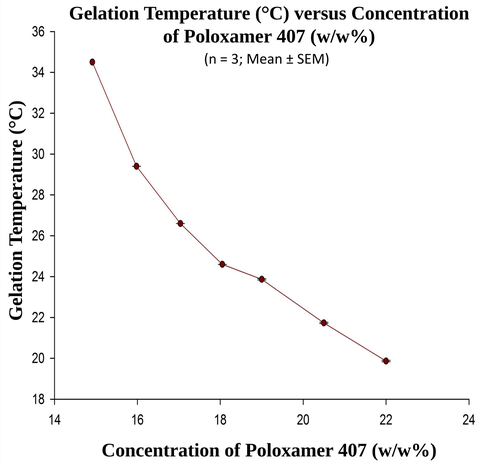
Saline	Pro	• Thermal insulator • Biocompatible
	Con	• Electrical conductor • Fluid migration • Barrier degradation
D5W	Pro	• Electrical insulator • Thermal insulator • Biocompatible
	Con	• Fluid migration • Barrier degradation
Ideal Hydrodissection Fluid	Additional Requirements	• Increased viscosity • Increased bioadhesion • Decreased fluid migration • Decreased barrier degradation

Final Design – 15.4 w/w% Poloxamer 407 (P407)



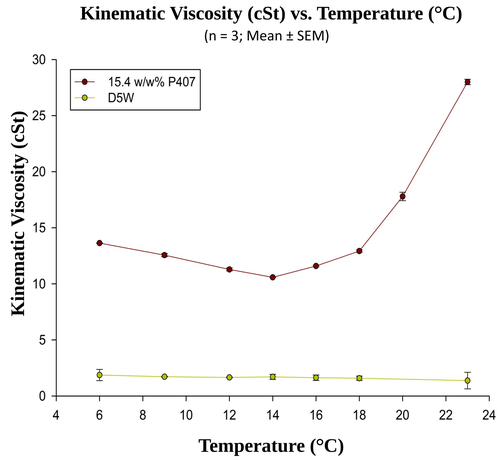
- ***Thermoreversible*** **- A poloxamer solution would be injected as a fluid which would then form a viscoelastic gel in vivo [5-7].**
- ***Bioabsorbable*** **– Poloxamer 407 would be absorbed by the body, processed through the kidneys (MW <13 kDa), and excreted through the urine [5-6].**
- ***Non-ionic*** **- Poloxamer 407 is non-ionic which suggests it will act as an electrical insulator [8].**
- ***Rapid Erosion*** **– The product is expected to be cleared from the body cavity in 48-72 hours [5].**
- ***Low mechanical strength*** **– This is expected to have no effect on the product efficacy since the patient is relatively immobile during ablation procedures [5].**

15.4 w/w% P407 Gels at 32°C



➢ **The use of 15.4 w/w% poloxamer solution would cause the poloxamer solution to gel at 32°C. When injected within the peritoneal cavity, this fluid would gel when raised to body temperature.**

P407 is More Viscous than D5W



➢ **The poloxamer solution has a viscosity 11x higher than D5W. The increase in viscosity retards fluid flow, suggesting the prevention of fluid migration within the peritoneal cavity.**

P407 does not Inhibit 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

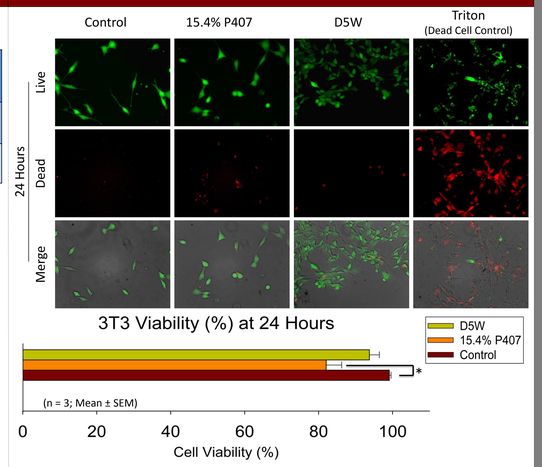
Ultrasound

D5W | Poloxamer Solution | Poloxamer Gelled

➢ **The use of the 15.4% poloxamer solution for hydrodissection would not inhibit imaging techniques used during ablation procedures.**

➢ **The addition of Iohexal, used to increase contrast during CT scans, does not inhibit gelation.**

P407 has Low Cytotoxicity



➢ **The addition of 15.4% P407 resulted in a reduction of cell viability 24 hours after exposure; however, this was not a significant compared to D5W.**

P407 Acts as a Protective Barrier

➢ **The 15.4 w/w% poloxamer solution and gel has an impedance comparable to D5W, which suggests the poloxamer solution will provide adequate electrical insulation during ablation.**

➢ **The high heat capacity of water suggests the P407 solution will form an effective thermal barrier.**

Sample	Impedance (Ω)
Blank	40
Saline	88
D5W	High (>1000)
15.4% P407 (solution)	High (>1000)
15.4% P407 (gel)	High (>1000)

Discussion

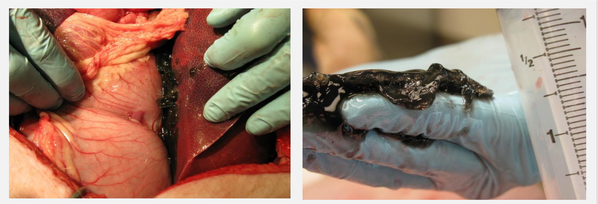
- **A 15.4 w/w% poloxamer 407 solution will gel at 32°C. The gelation temperature may be altered to optimize in vivo gelation.**
- **Poloxamer is able to be differentiated from tissues during CT scan and is ultrasound transparent. The effects of Iohexal on the P407 solution (i.e. change in gelation temperature) have not yet been evaluated.**
- **A 15.4 w/w% poloxamer solution will act as an adequate electrical insulator to protect tissue during RF ablation procedures. Although adequate thermal protection is expected, heat transfer through the P407 solution was not evaluated.**
- **The increase in viscosity suggests the 15.4% poloxamer solution will prevent fluid migration and barrier degradation. It is expected < 250 mL of solution will provide adequate protection.**
- **Live/dead assay results suggest the 15.4% P407 solution causes a cellular response. This was not significant compared to currently used D5W. Further toxicity testing is to be conducted to further evaluate potential toxicity.**

Conclusion

A 15.4 w/w% poloxamer has characteristics similar to current hydrodissection fluids (i.e. D5W, 0.91% NaCl) but would prevent fluid migration and barrier degradation during ablation procedures. To efficiently inject the viscous solution, it is recommended that the solution be cooled below 18°C prior to hydrodissection.

Future Work

- **Rheometry testing**
- **Tissue phantom testing**
- **Animal testing**



- **WARF Disclosure/Patenting**
- **Additional toxicity testing**
- **FDA approval**
- **Clinical trials**

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- **Dr. Eric Codner**
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9) L. Hinshaw, et al., *The Roll of Image-guided Tumor Ablation in the Management of Liver Cancer.* Available: http://www.cancernews.com/data/Article/504.asp

Images

- Tissues – From [4]
- Hepatic Tumor Ablation – From [9]
- Poloxamer micellization – From [6]