

Absorbable Hydrodissection Fluid

Group Members:

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Advisor:

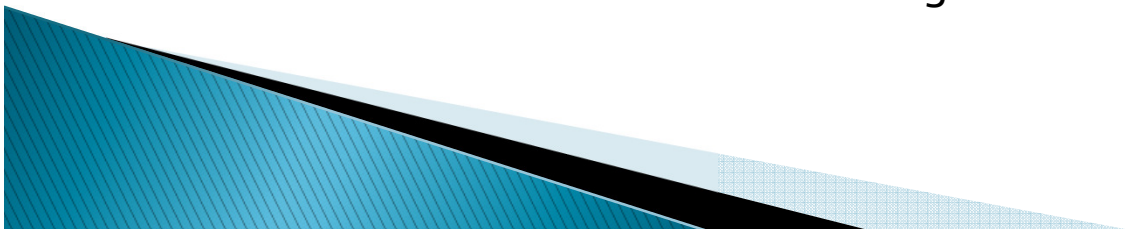
Dr. John Puccinelli

Client:

Dr. Chris Brace

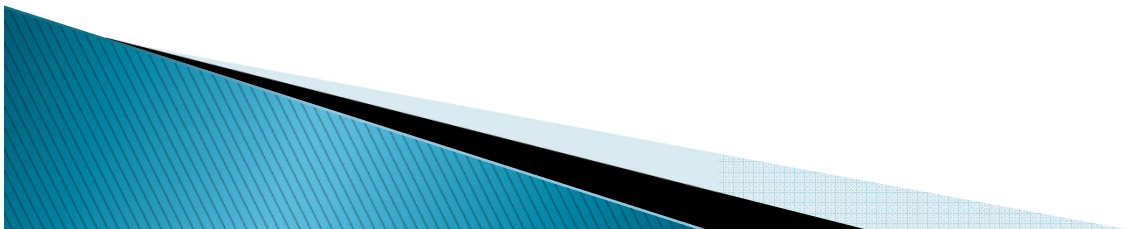
Dr. J. Louis Hinshaw

Dr. Meghan Lubner



Problem Motivation

- ▶ Over 500,000 new incidences of liver cancer annually
- ▶ Ablation used to treat tumors
 - Unwanted tissue damage
- ▶ Hydrodissection fluid separates tissues
 - Unintended migration
 - Quick absorption
 - Barrier degradation
 - Leads to excess liquid use



Radiofrequency (RF) Ablation



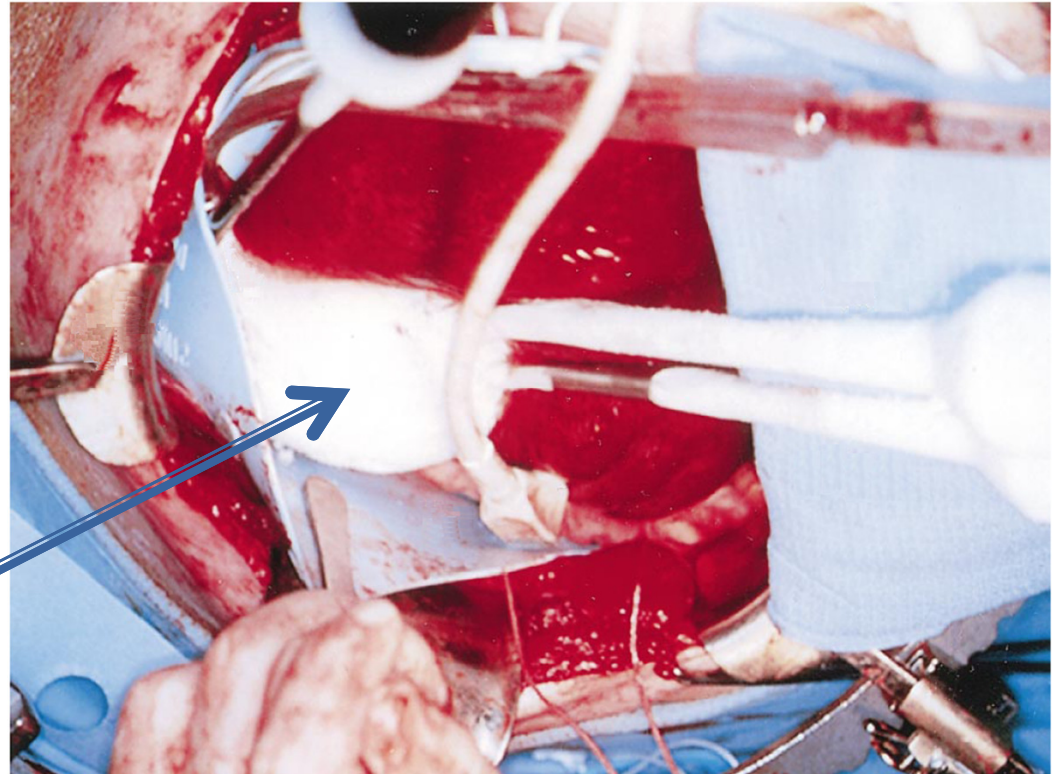
- ▶ Uses RF AC current to generate heat in an electrode and ‘burn out’ tumors
- ▶ Few patient complications
- ▶ > 85% success in eliminating tumors

G. D. D. III, *et al.*, "Minimally Invasive Treatment of Malignant Hepatic Tumors: At the Threshold of a Major Breakthrough," *RadioGraphics*, vol. 20, p. 19, 2000

Cryoablation

- ▶ Freezes target tissue
- ▶ Can treat larger tumors than RFA
- ▶ Better control

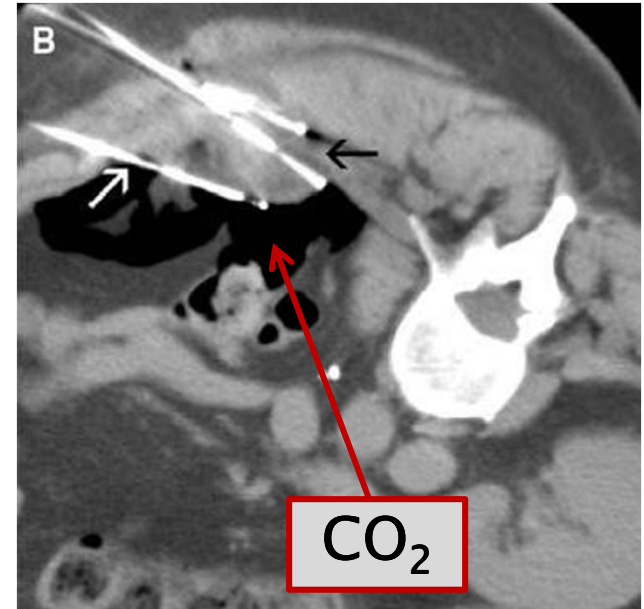
ICE BALL



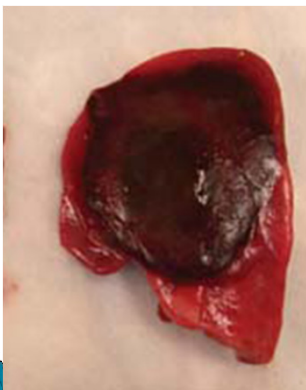
Adapted from G. D. D. III, *et al.*, "Minimally Invasive Treatment of Malignant Hepatic Tumors: At the Threshold of a Major Breakthrough," *RadioGraphics*, vol. 20, p. 19, 2000

Current Treatments

- ▶ 5% Dextrose in Water (D5W)
- ▶ CO₂ gas bladder or insufflation
- ▶ Saline



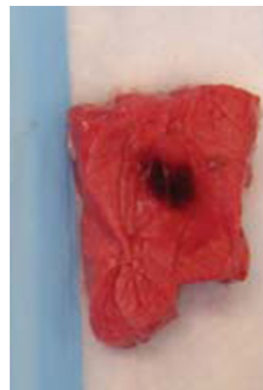
No Treatment



Saline



D5W



Adapted from Buy, X, et al., *Thermal protection during percutaneous thermal ablation procedures: interest of carbon dioxide dissection and temperature monitoring*, Cardiovascular and interventional radiology, 2009. **32**(3): p. 529-534.

Adapted from P. F. Laeske, et al., "Unintended injuries from radiofrequency ablation: Protection with 5% dextrose in water," *Am. J. Roentgenology*, vol. 186, pp. 5249-5254, 2006.

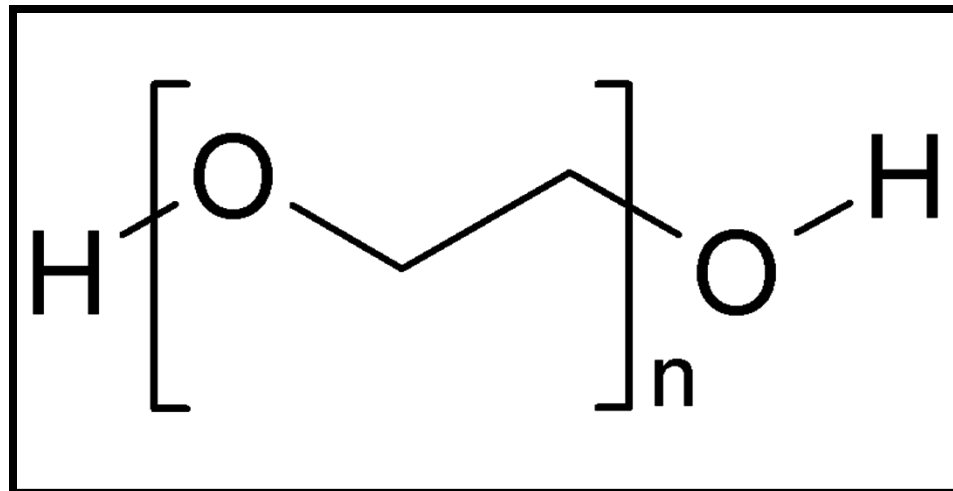
Design Specifications

- ▶ Easy to inject
- ▶ Visible with imaging techniques
 - Ultrasound
 - CT/MRI
- ▶ Biocompatible
- ▶ Insulator
 - Thermal
 - Electrical
- ▶ Less than \$200



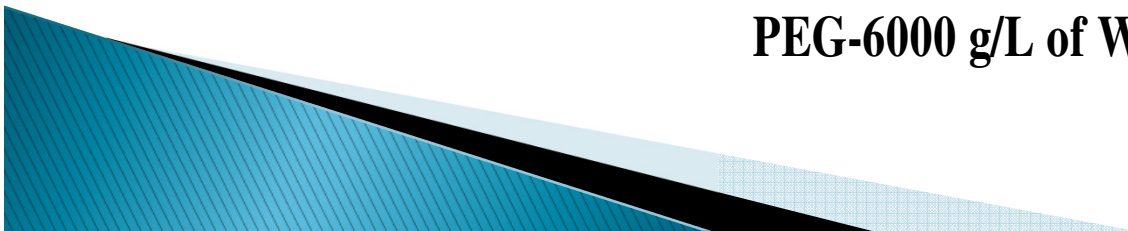
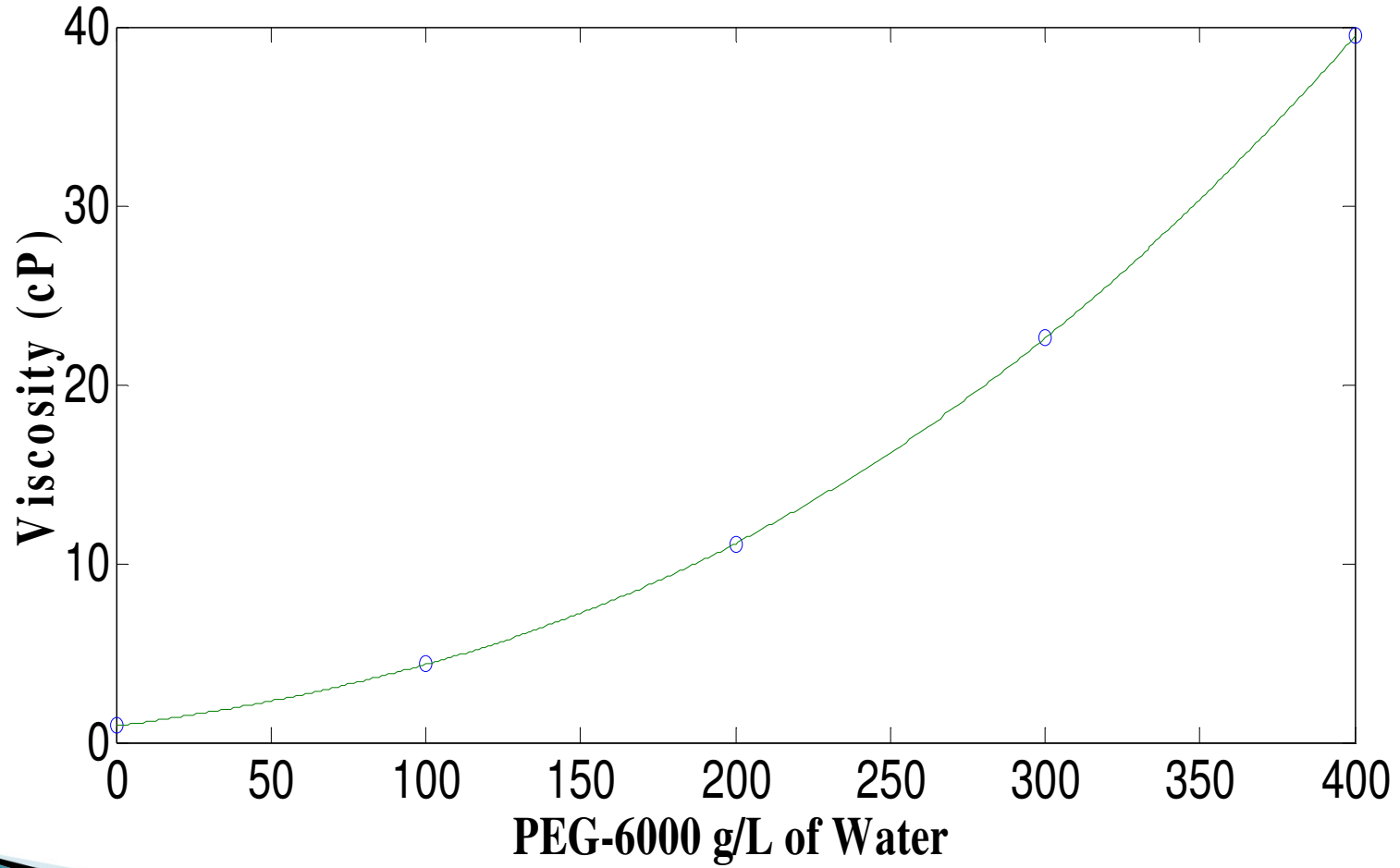
Poly(ethylene glycol) – PEG

- ▶ History – additive
- ▶ Biologically inert
- ▶ FDA approved
- ▶ Viscosity is concentration dependent



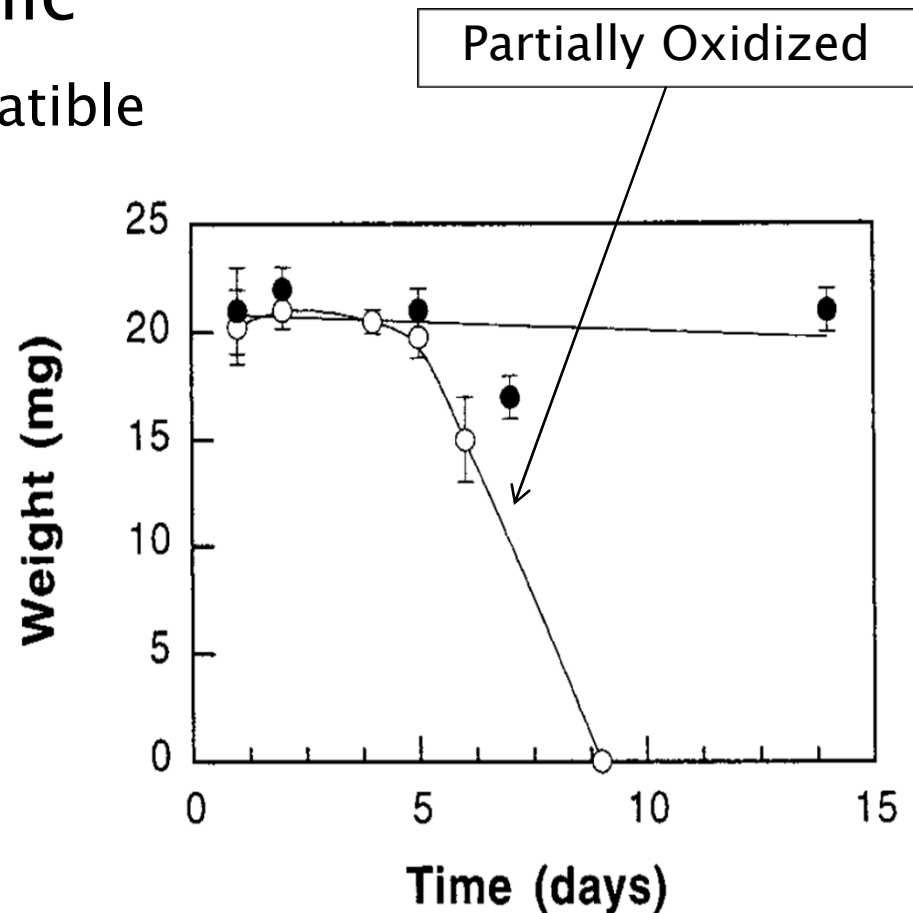
PEG

Viscosity of Various Concentrations of PEG Solutions at 25 Degrees Celsius



Sodium Alginate

- ▶ Natural: non-antigenic
 - Biodegradable, biocompatible
- ▶ Degradation rate
 - Control with partial oxidation
- ▶ Instant gelation
 - Ionic crosslink
- ▶ Two injections



http://bme.case.edu/libraries/Document/alsberg_lab/bouhadir.biot echprog.2001.pdf

Sodium Alginate Injections

▶ Three Injections

1. CaCl_2
2. D5W Flush
3. Sodium Alginate

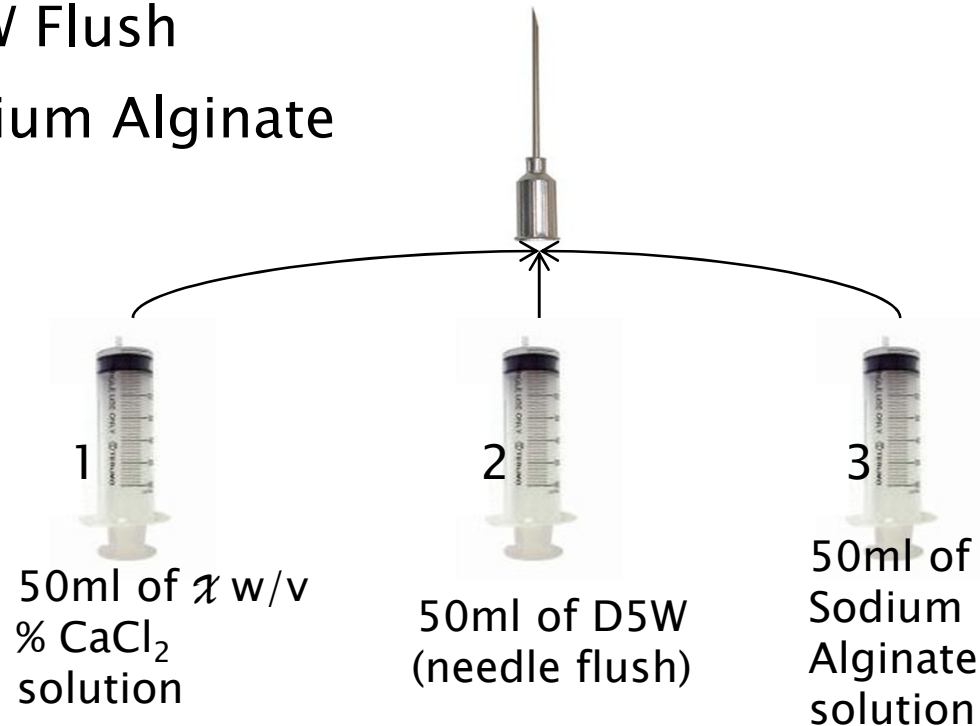


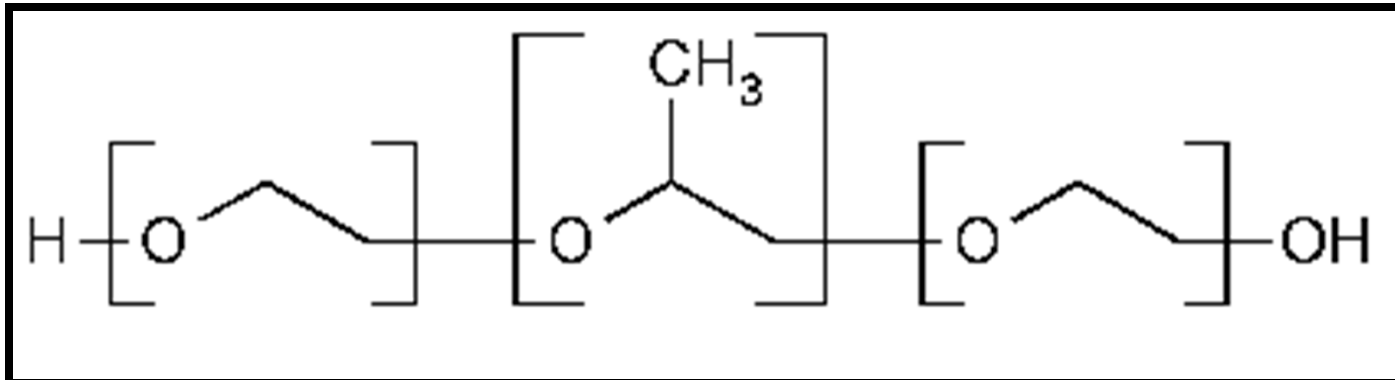
Image from Syringe - <http://www.ausjetinks.com.au/p/50ml-Syringe-Eccentric-Tip/Syringes-Injectors/INK-30-SYRINGE50ML>

20 gauge needle -

http://www.ekosmet.com/index.php?language=product_info&cPath=1_54_116&products_id=551&zenid=6d7de31218abb4cc13c05c28571b3dbe

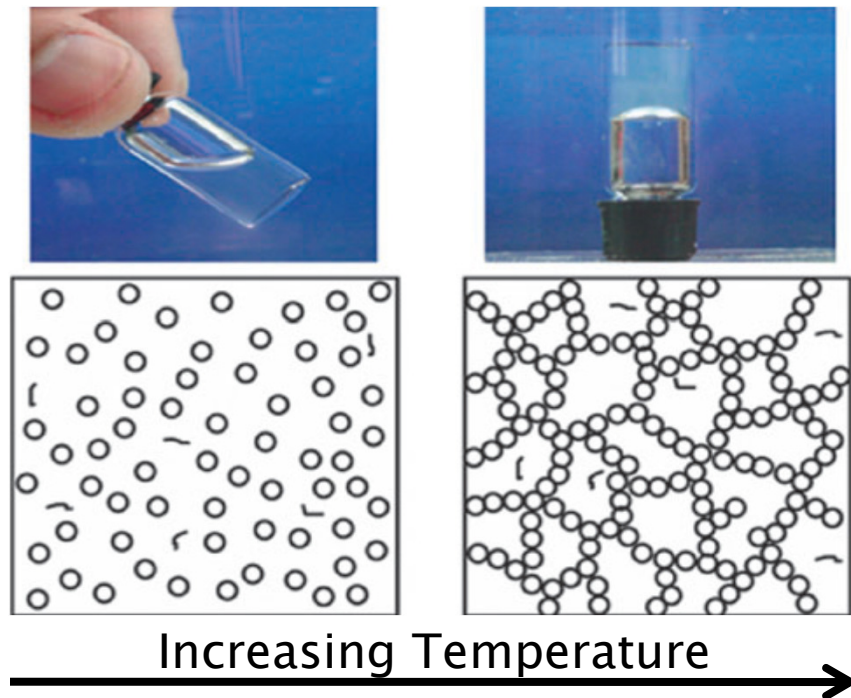
Poloxamer

Poly(ethylene oxide)-*b*-poly(propylene oxide)-*b*-poly(ethylene oxide) or PEO-PPO-PEO triblock copolymer



Poloxamer 407

- ▶ Thermoreversible solution to gel phase change
- ▶ Considered bioabsorbable if MW < 13kDa
- ▶ Low mechanical strength
- ▶ Rapid erosion
- ▶ Non-ionic



Adapted from L. Yu and J. Ding, "Injectable hydrogels as unique biomedical materials," *Chemical Society Reviews*, vol. 37, pp. 1473–1481, 2008.

Poloxamer Testing

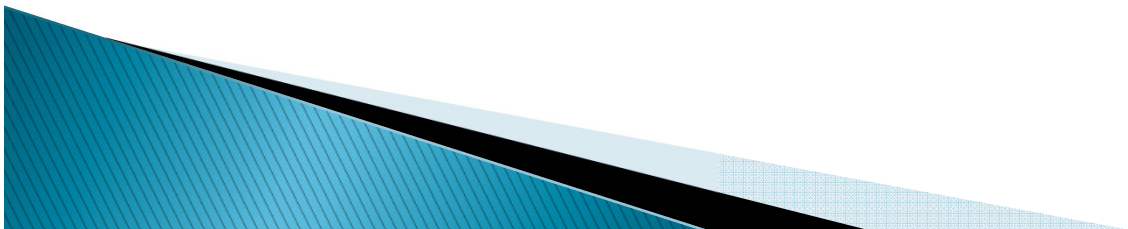
- ▶ Determine concentration (w/v%) and gelation temperature relationship

Concentration (w/v %)	Gelation Temp (°C)
15	N/A
17.5	N/A
18.75	N/A
20	25.7 ± 1.5
22.5	23.1 ± 0.3



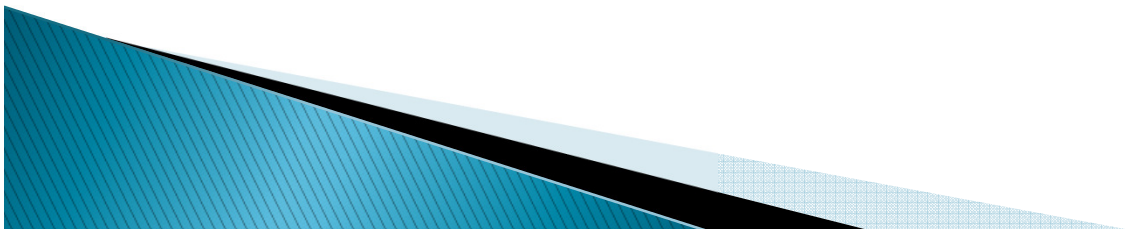
Design Matrix

	Poly(ethylene glycol)	Poloxamer 407 Gel	Sodium Alginate Gel
Biocompatibility (30pts)	30	25	20
Viscosity (20pts)	15	20	20
Cost of Materials (10 pts)	5	10	5
Ergonomics (15 pts)	10	15	5
Temperature Range (25 pts)	25	20	25
Total	85	90	75



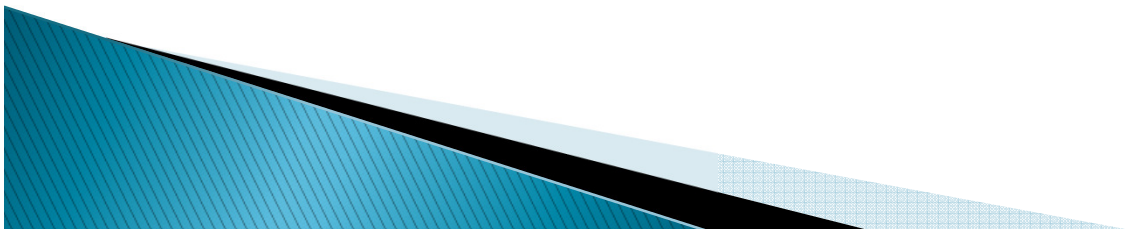
Future Work

- ▶ Testing
 - Concentration
 - Tissue-equivalent phantoms
- ▶ Optimization
 - Viscosity
 - Imaging contrast
- ▶ Cost
 - Lab supplies: \approx \$30
 - Estimated cost of product: \$10/unit

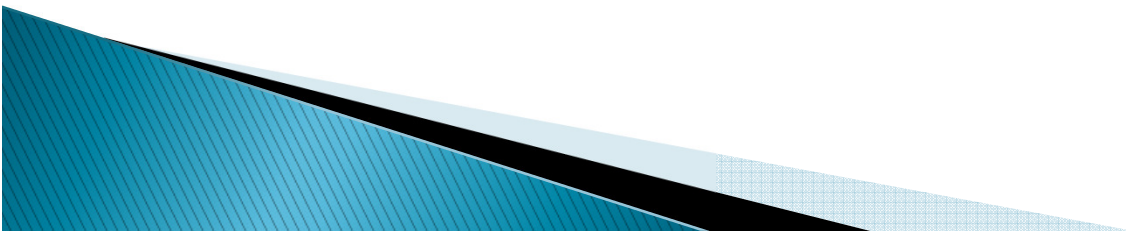


Acknowledgements

- ▶ Dr. John Puccinelli
- ▶ Dr. Chris Brace
- ▶ Dr. James Hinshaw
- ▶ Dr. Meghan Lubner
- ▶ Dr. William Murphy



Questions?



References

1. B. Michel and M. Kaufmann, "The osmotic potential of polyethylene glycol 6000," *Plant physiology*, vol. 51, p. 914, 1973.
2. F. Veronese and G. Pasut, "PEGylation, successful approach to drug delivery," *Drug Discovery Today*, vol. 10, pp. 1451–1458, 2005.
3. S. Zalipsky, "Chemistry of polyethylene glycol conjugates with biologically active molecules," *Advanced Drug Delivery Reviews*, vol. 16, pp. 157–182, 1995.
4. Brace, C., et al. Electrical isolation during radiofrequency ablation: 5% dextrose in water provides better protection than saline. 2008: IEEE.
5. Dodd, G., et al., Minimally Invasive Treatment of Malignant Hepatic Tumors: At the Threshold of a Major Breakthrough1. *RadioGraphics*, 2000. 20(1): p. 9.
6. Buy, X., et al., Thermal protection during percutaneous thermal ablation procedures: interest of carbon dioxide dissection and temperature monitoring. *Cardiovascular and interventional radiology*, 2009. 32(3): p. 529–534.
7. L. Yu and J. Ding, "Injectable hydrogels as unique biomedical materials," *Chemical Society Reviews*, vol. 37, pp. 1473–1481, 2008.
8. K. Y. L. Kamal H. Bouhadir, Eben Alsberg, Kelly L. Damm, Kenneth W. Anderson, David J. Mooney. (2001, 10/5/2010). Degradation of Partially Oxidized Alginate and Its Potential Application for Tissue Engineering. *Biotechnology Program 17(5)*, 945–950. Available: <http://onlinelibrary.wiley.com.ezproxy.library.wisc.edu/doi/10.1002/jcp.1041520225/abstract>
9. C. Sheeham. October 9). *Poloxamer*. Available: http://www.uspbpep.com/usp28/v28230/usp28nf23s0_m66210.htm
10. G. Dumortier, *et al.*, "A review of poloxamer 407 pharmaceutical and pharmacological characteristics," *Pharmaceutical research*, vol. 23, pp. 2709–2728, 2006.
11. S. Singh–Joy and V. McLain, "Safety assessment of poloxamers 101, 105, 108, 122, 123, 124, 181, 182, 183, 184, 185, 188, 212, 215, 217, 231, 234, 235, 237, 238, 282, 284, 288, 331, 333, 334, 335, 338, 401, 402, 403, and 407, poloxamer 105 benzoate, and poloxamer 182 dibenzoate as used in cosmetics," *International journal of toxicology*, vol. 27, p. 93, 2008.
12. B. Fussnegger. (2000, October 8). *Poloxamers (2)*. Available: http://worldaccount.basf.com/wa/NAFTA/Catalog/Pharma/doc4/BASF/exact/lutrol_f_127/.pdf?title=Poloxamers%20%28%29%20Lutrol%20F%20127%20%28Poloxamer%20407%29.&asset_type=pi/pdf&language=EN&urn=urn:documentum:eCommerce_sol_EU:09007bb28001ac1d.pdf

