Medical Device Applications of Shape Memory Polymers

D.J. Maitland[1],

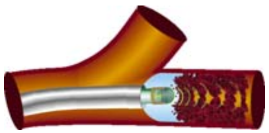
T. Wilson[1], W. Small[1], J. Bearinger[1], J. Ortega[1],
J. Van de Water[2] and J. Hartman[2]

[1] Medical Technology Program, Lawrence Livermore National Laboratory
[2] University of California at Davis Medical Center

September 23, 2007

Introduction: MTP interventional device history

Endovasix CRADA
Optoacoustic thrombolysis
PI(s): Matthews/Da Silva



ENG Techbase
SMP
thrombectomy
PI(s): Maitland

IIC CRADA
X-ray Catheter
PI(s): Trebes

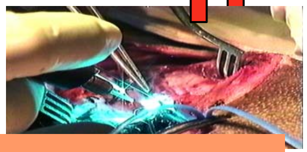
NIH BRP, SMP for stroke PI(s): Maitland, Wilson, Hartman, Van de Water

NIH R21 Biomaterials
PI(s): Bearinger

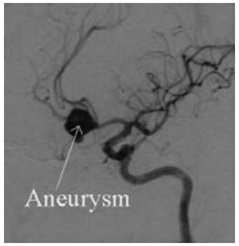
LDRD-LW SMP
Materials
PI(s): Wilson

1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007

Stroke LDRD
PI(s):
Fitch/Matthews



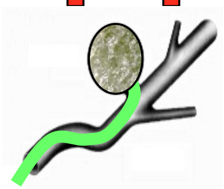
CEE CRADA
Laser-tissue
welding
PI(s): Matthews/
Maitland



Micrus CRADA
SMP embolic coil
release
PI(s): Da Silva/Lee

DOE Pilot Grant
SMP
thrombectomy
PI(s): Maitland

CBST SMP
biocompatibility
PI(s): Maitland/Van
de Water



Sierra
CRADA
SMP foams
PI(s):
Maitland

LDRD-ER
Vascular Devices
PI(s): Maitland

NSF SMP
aneurysm
PI(s):
Hartman/Maitland

LDRD – laboratory directed research & development funding
CRADA – cooperative research & development agreement

Part I

SMP Background

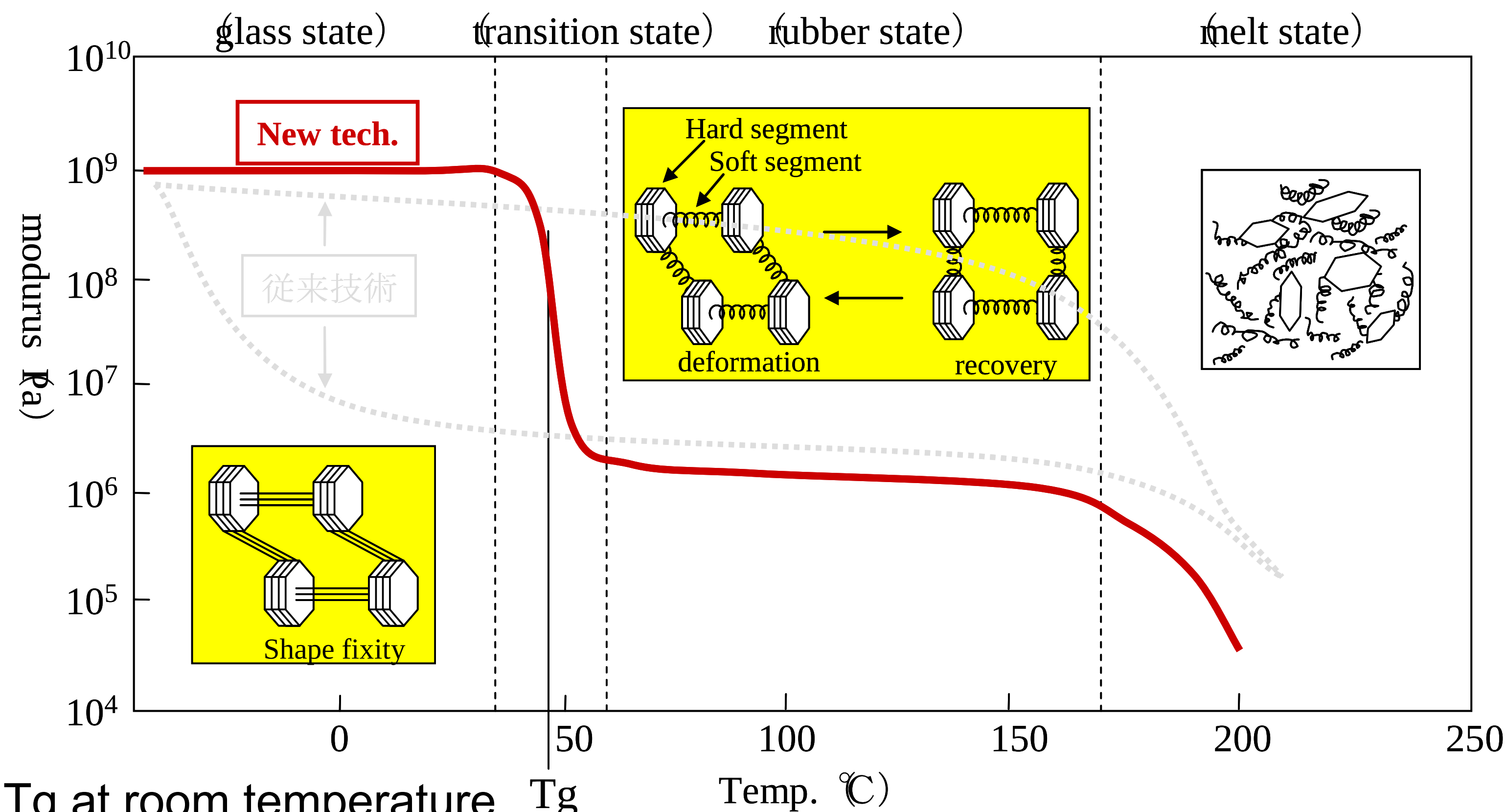
Shape memory example: thermally activated polyurethane

SMP is fabricated into primary shape

Deformed above Tg, then cooled to fix secondary shape

Actuated back into primary shape by controlled heating

Shape memory example: thermally activated polyurethane



- Tg at room temperature
- Narrow transition state
- Drastic change of properties at transition state

Courtesy of S. Hayashi

History of SMPs

1951
SMA Chang & Read
J. Met.

1990s
Commercial Sales
Diaplex
Polyurethane

1940	1950	1960	1970	1980	1990

1941
US2234993
L.B. Vernon
Dental App.

1960s
Heat
Shrink
Tubing

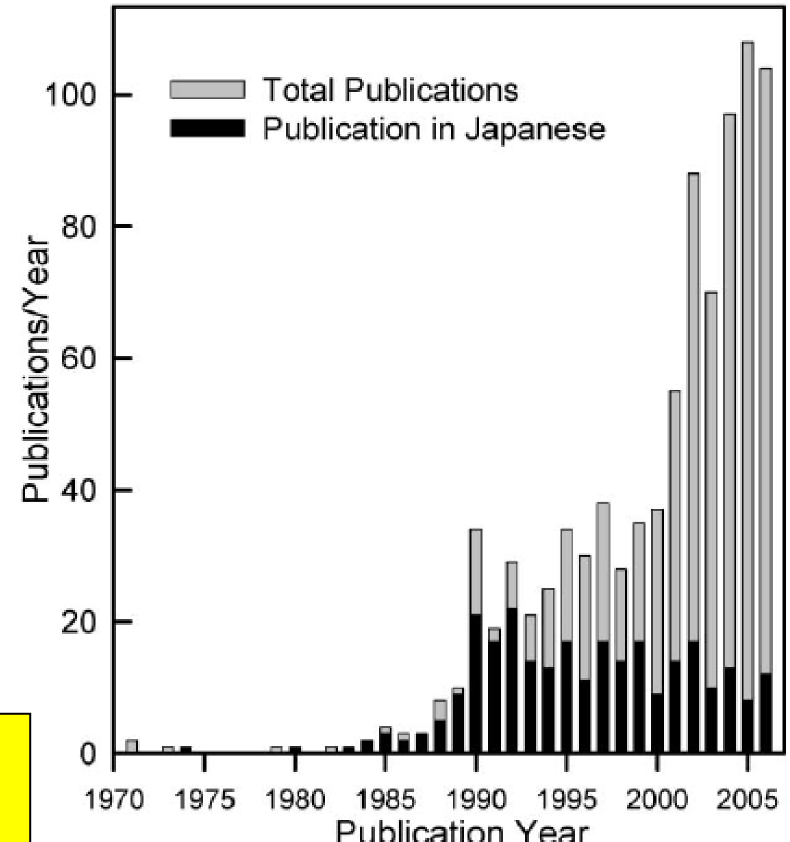
1980s
Multiple
Groups
(Japan)

1996
Human
Trials
Embolic
Coil
Release

Review Articles:
*Liu, Qin and Mather, *J. Mater. Chem.* 2007
Behl and Lendlein, *Mater. Today* 2007

While shape memory is inherent to many polymers, targeted engineering of SMP properties has increased over the last 20 years.

Publication History of SMPs
(from Liu, Qin and Mather, *J. Mater. Chem.* 2007)



Types of SMPs and activation mechanisms

Types of SMPs

*Type I: Chemically cross-linked glassy Thermosets

Type II: Chemically cross-linked semi-crystalline rubbers

Type III: Physically cross-linked thermoplatics

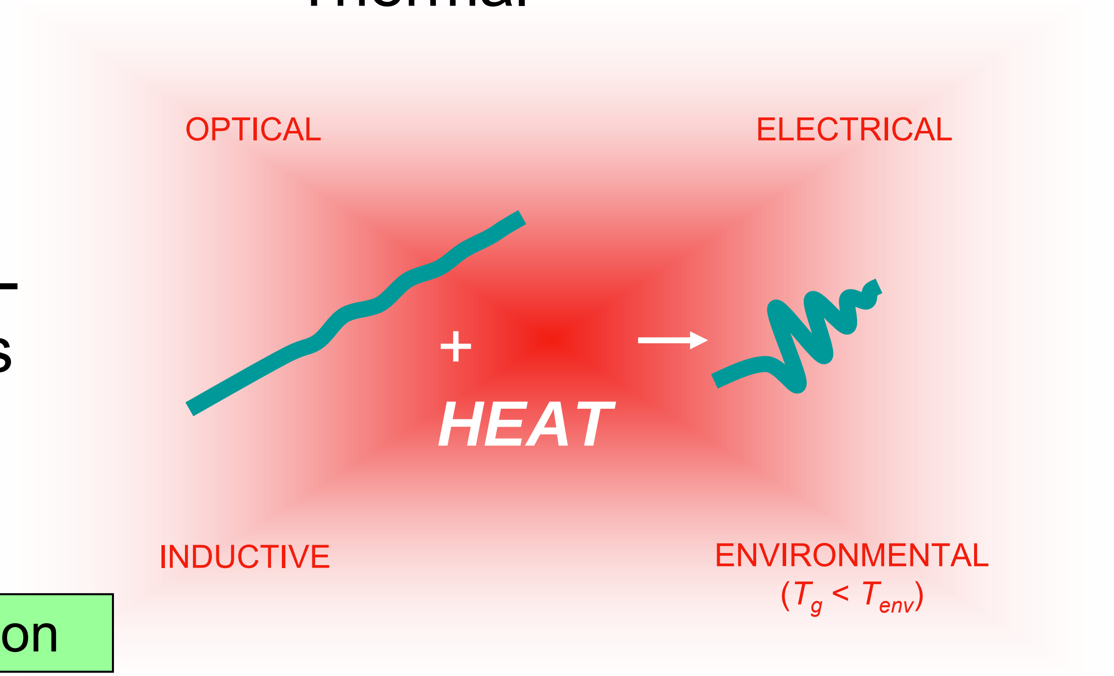
*Type IV: Physically cross-linked block copolymers

(Liu, Qin and Mather, *J. Mater. Chem.* 2007)

Bi-stable, unidirectional actuation

Activation Mechanisms

- Chemical
- Photo
- *Thermal

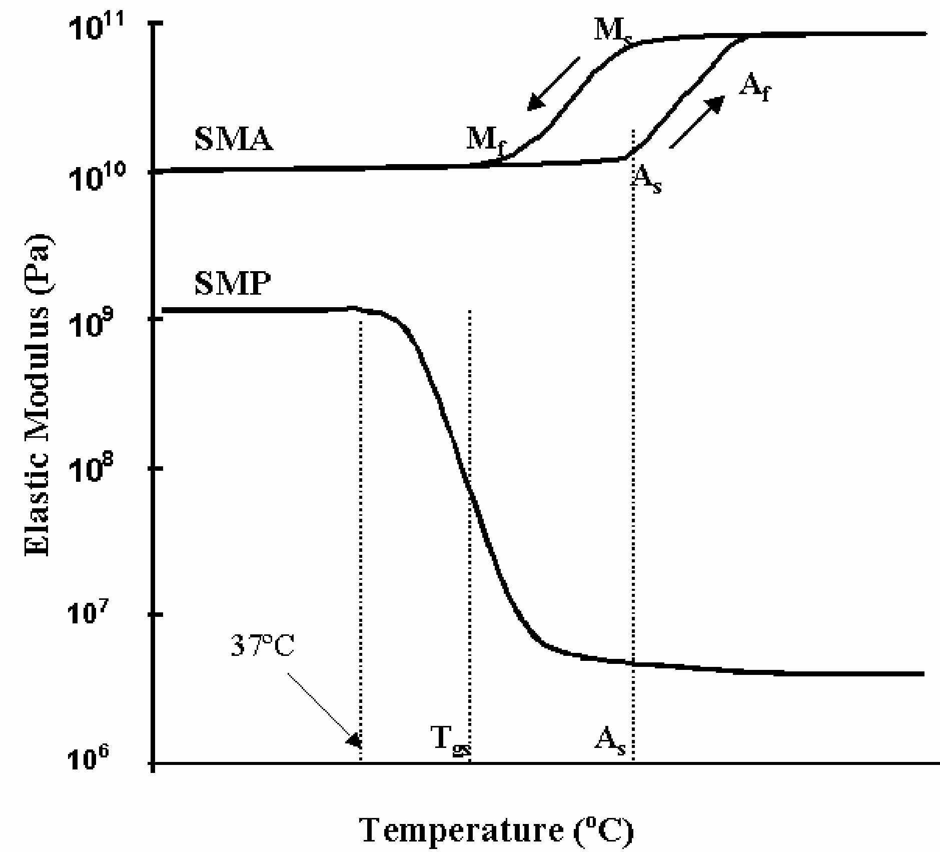


SMP properties

Comparison with shape memory alloy (SMA)

	SMP	**SMA**
Strain	**300%**	**10%**
ΔE	**>500x**	**10x**
Stress	**~25 MPa**	**~500 MPa**

(Hayashi et al., *Plast. Eng.* **7** 1995)



- Desired SMP features: sharp transition temperature, superelastic (low loss modulus, high strain recovery), rapid & complete fixing
- Other: variable Tg, optically clear, imaging contrast, biocompatibility

SMP enables complex geometries and shapes

SMP foam for treating aneurysms
(chemically blown, open cell foam)

Basket for catching large emboli
(micro-injection molded)

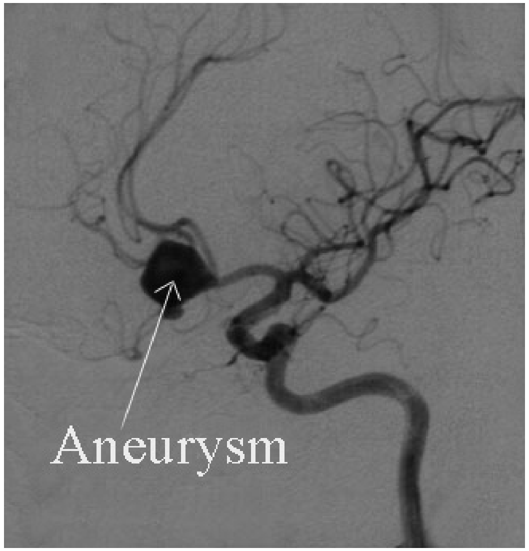
SMP stent
(dip coated and laser machined)

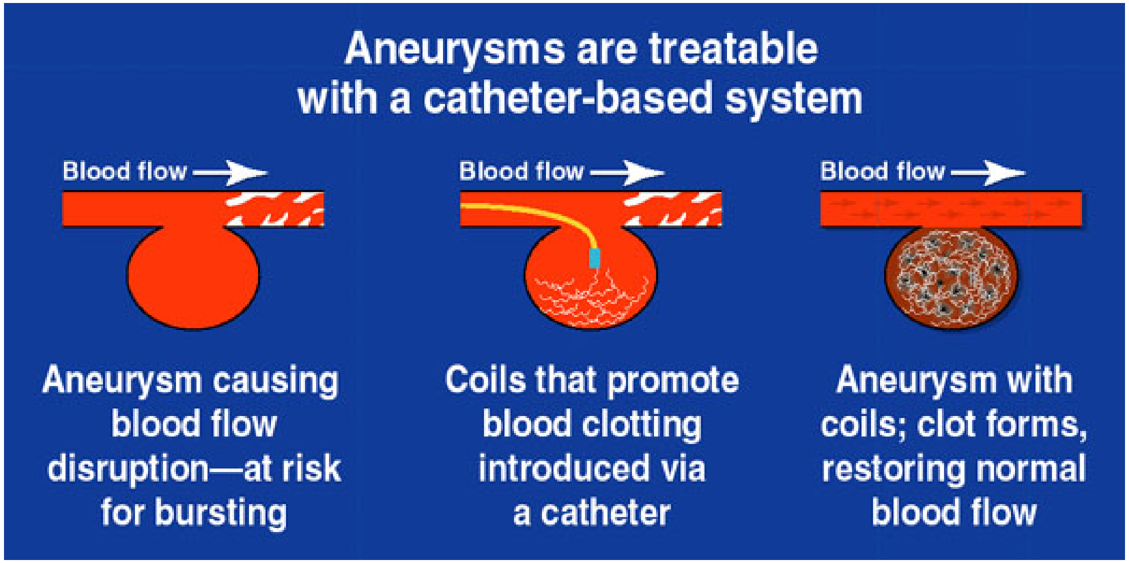
smp.llnl.gov

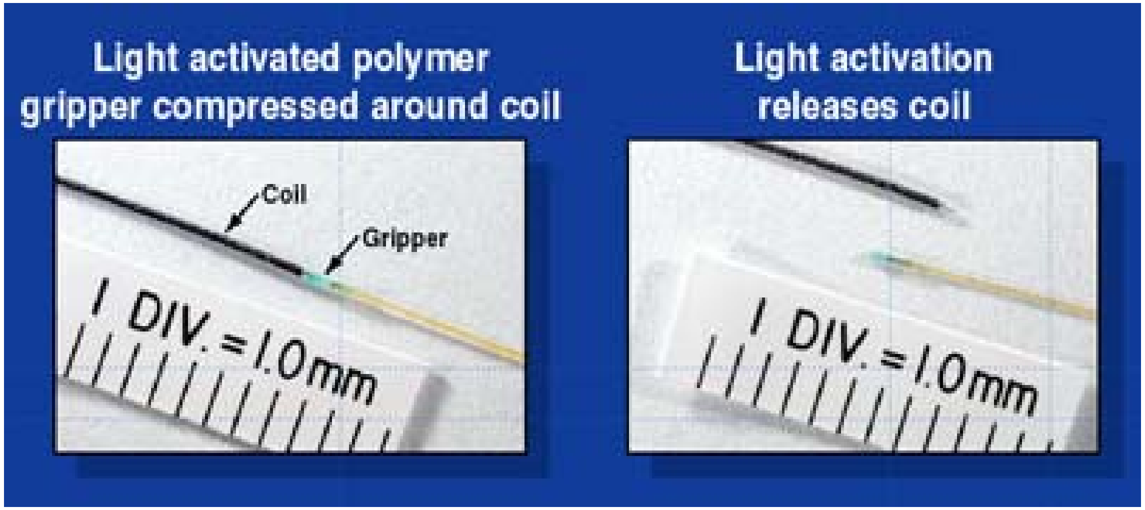
Part II

Medical Applications

1996: Treating potential hemorrhagic stroke with a SMP coil release system

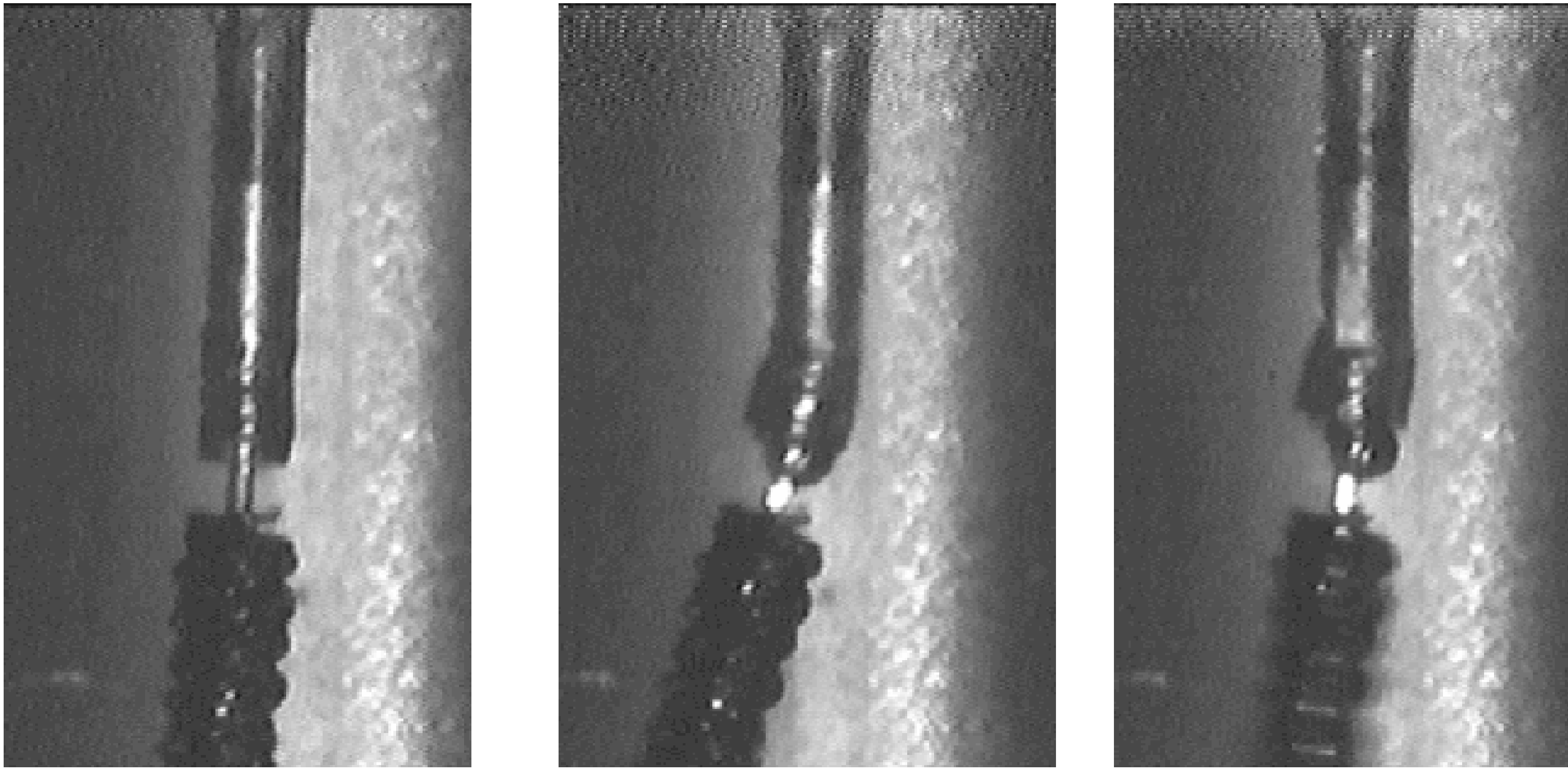






Maitland et al.,
US Patent 6,102,917, 1998

Embolic coil release: first SMP device in human trials



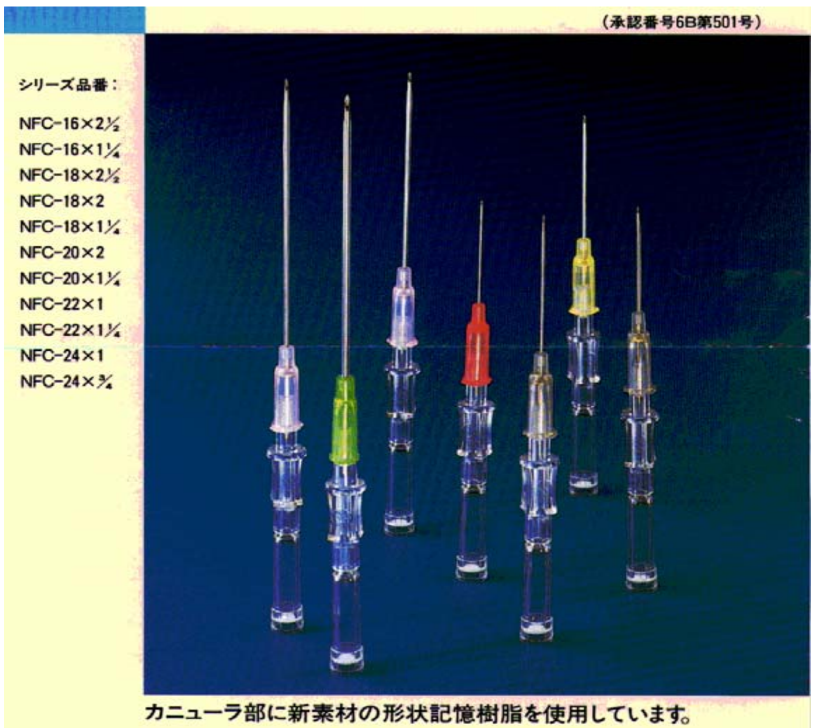
0 ms 133 ms 267 ms

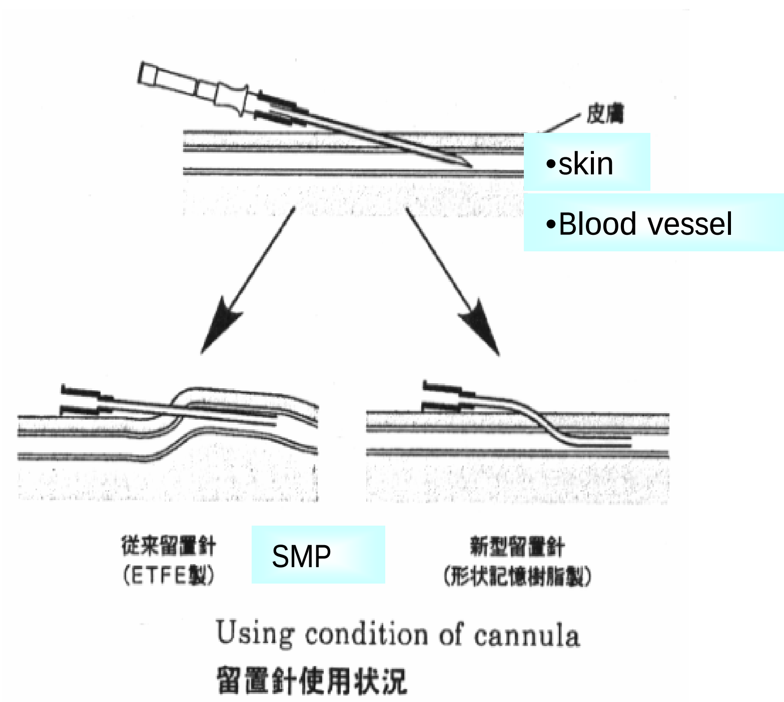
100 ml/min flow rate, 37 C

Courtesy of S. Hayashi

Intravenous syringe cannula

When injection is performed, it keeps its rigid state. Once under the skin, it becomes flexible, resulting in greater comfort.



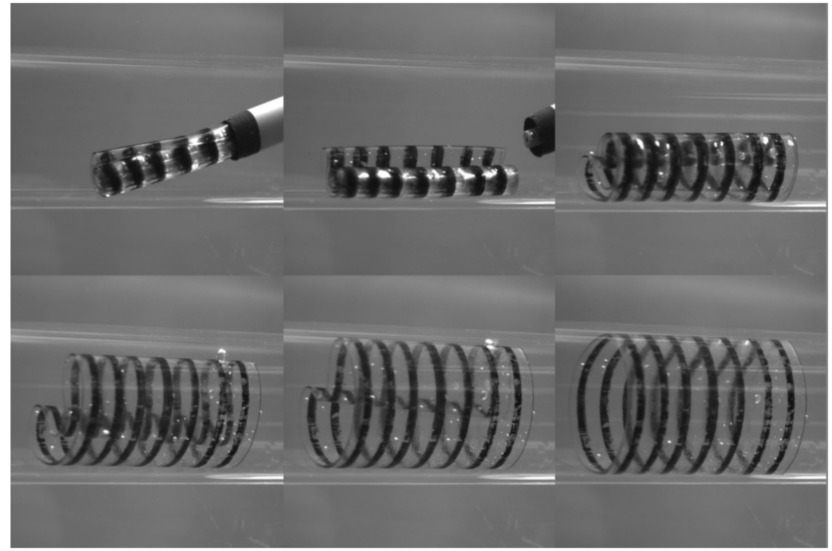


From Nipro

Courtesy of K. Gall

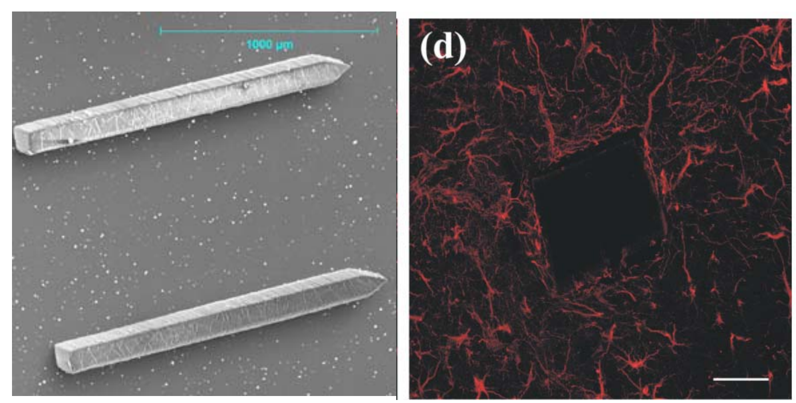
Target biomedical applications

- Cardiovascular Stents
  - Delivery via shape memory effect
  - Match mechanical properties of artery
  - Complex geometries to match arteries
  - Funding: NIH
  - Student: Chris Yakacki



Deployment of a SMP Stent from a Catheter

- Neuronal Probes
  - Slow deployment into tissue
  - Minimize tissue damage
  - Deployment past scar
  - Funding: NIH
  - Student: Scott Kasprazak



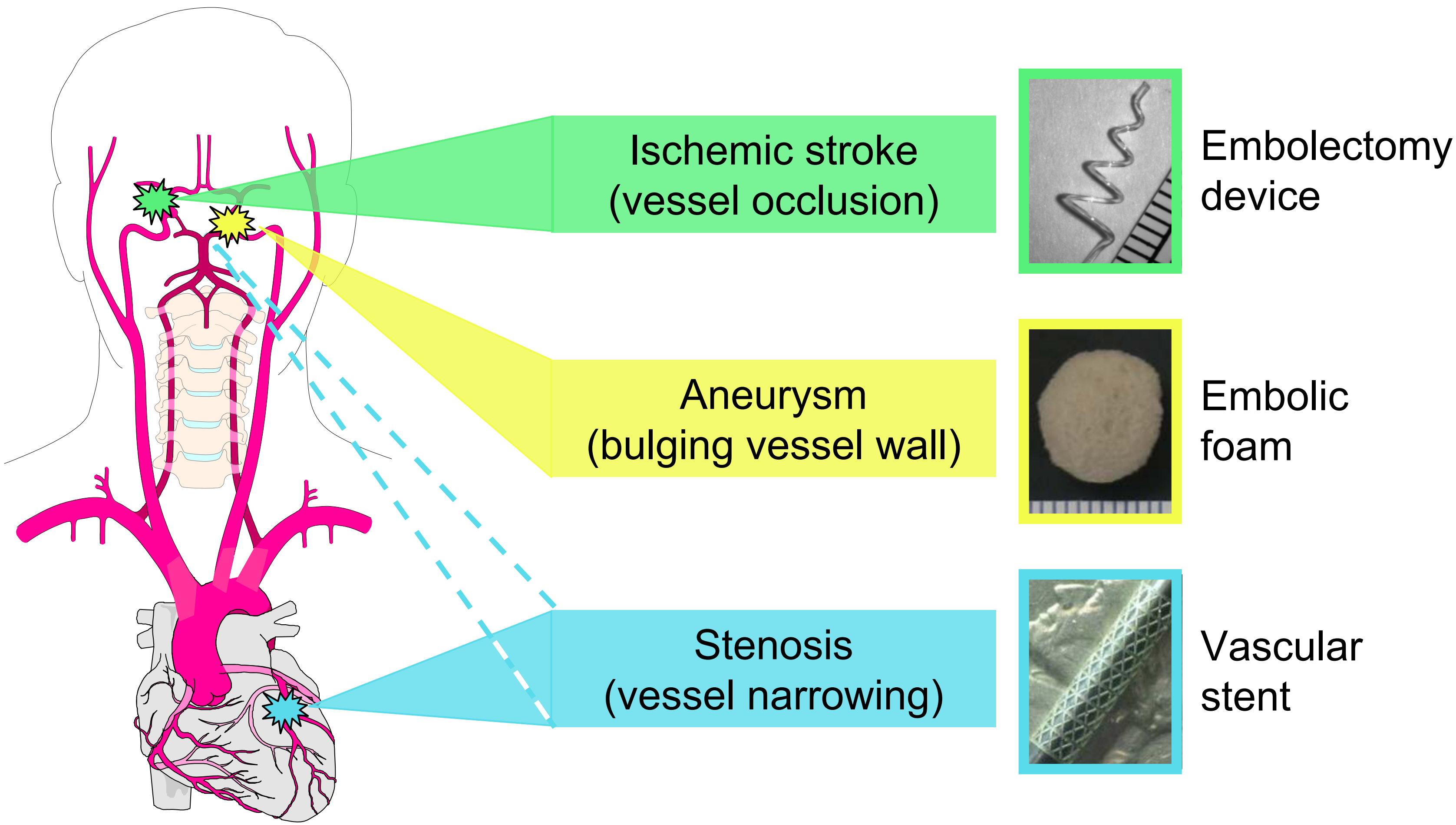
SMP Probe (left) and tissue response (right)

Other groups working on SMP medical applications

- Biodegradable stents, sutures – Lendlein & Langer
- Orthodontic implants – Mather
- SMP foams for aneurysms – Metcalf & Sokolowski
- Stents – Shandas & Gall

Behl and Lendlein, *Mater. Today* 2007

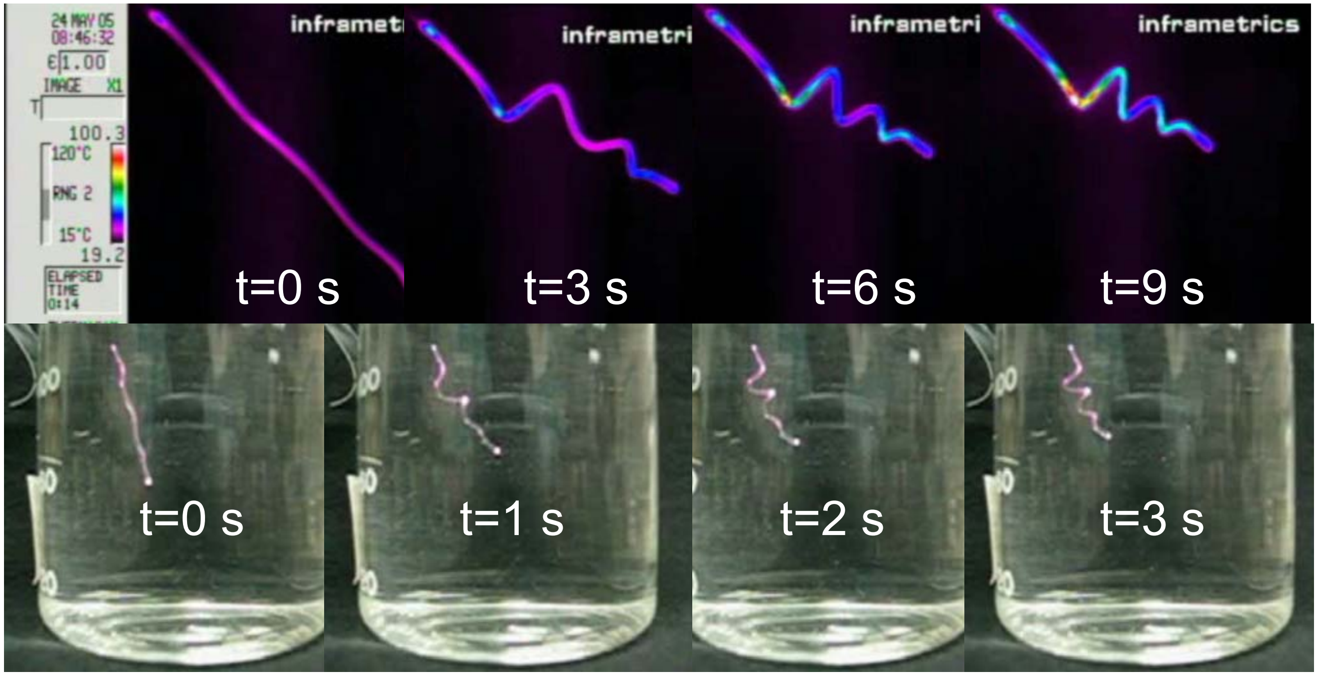
Interventional applications of SMP devices



Low force recovery forced redesign of embolectomy device

air
0.6 W

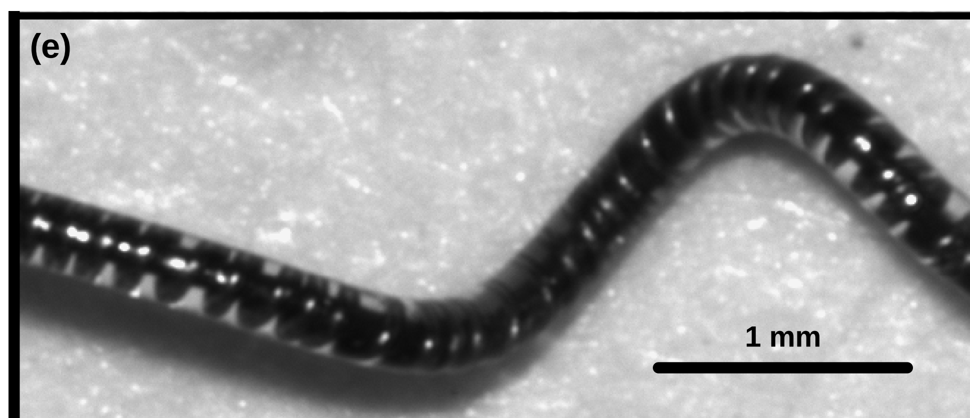
37 °C
water
zero flow
4.9 W



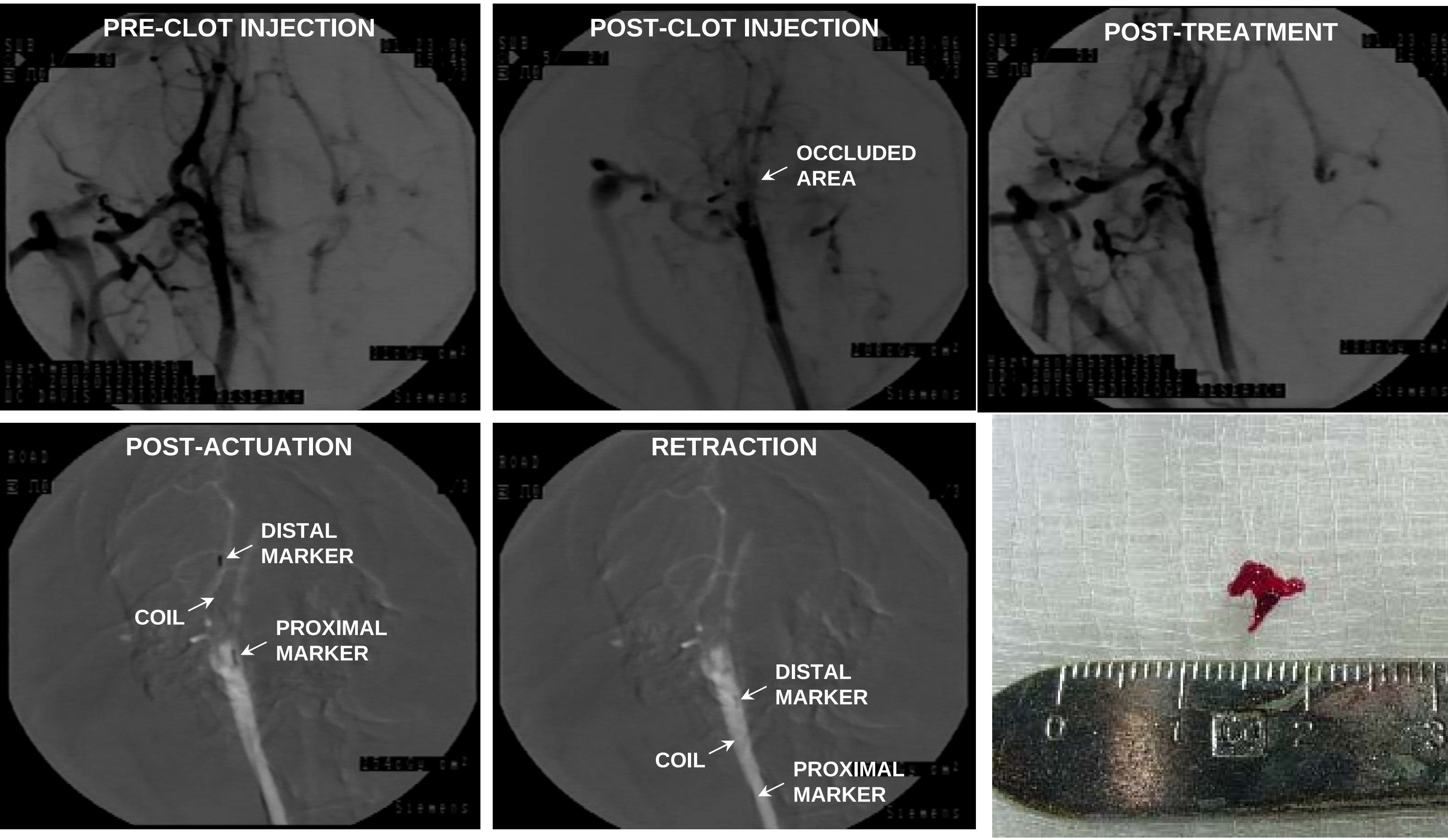
Maitland et al. *Lasers Surg. Med.* (2002)
Metzger et al. *J. Biomed. Micro Dev.* (2002)
Small et al. *IEEE Trans Quant. Elec.* (2005)

Hybrid
SMP-SMA,
resistively
actuated

Small et al. *IEEE Trans Biomed Eng* (2007)



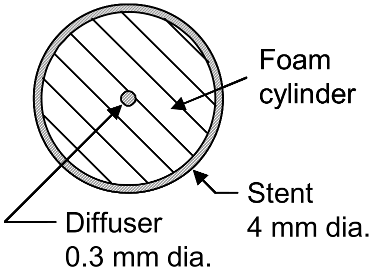
In vivo deployment of SMP-nitinol embolectomy device

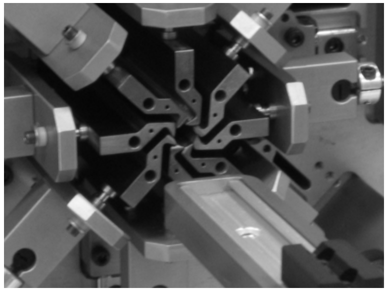


Hartman et al. *Am J Neuroradiol* (2007)

Fabrication of SMP vascular stent

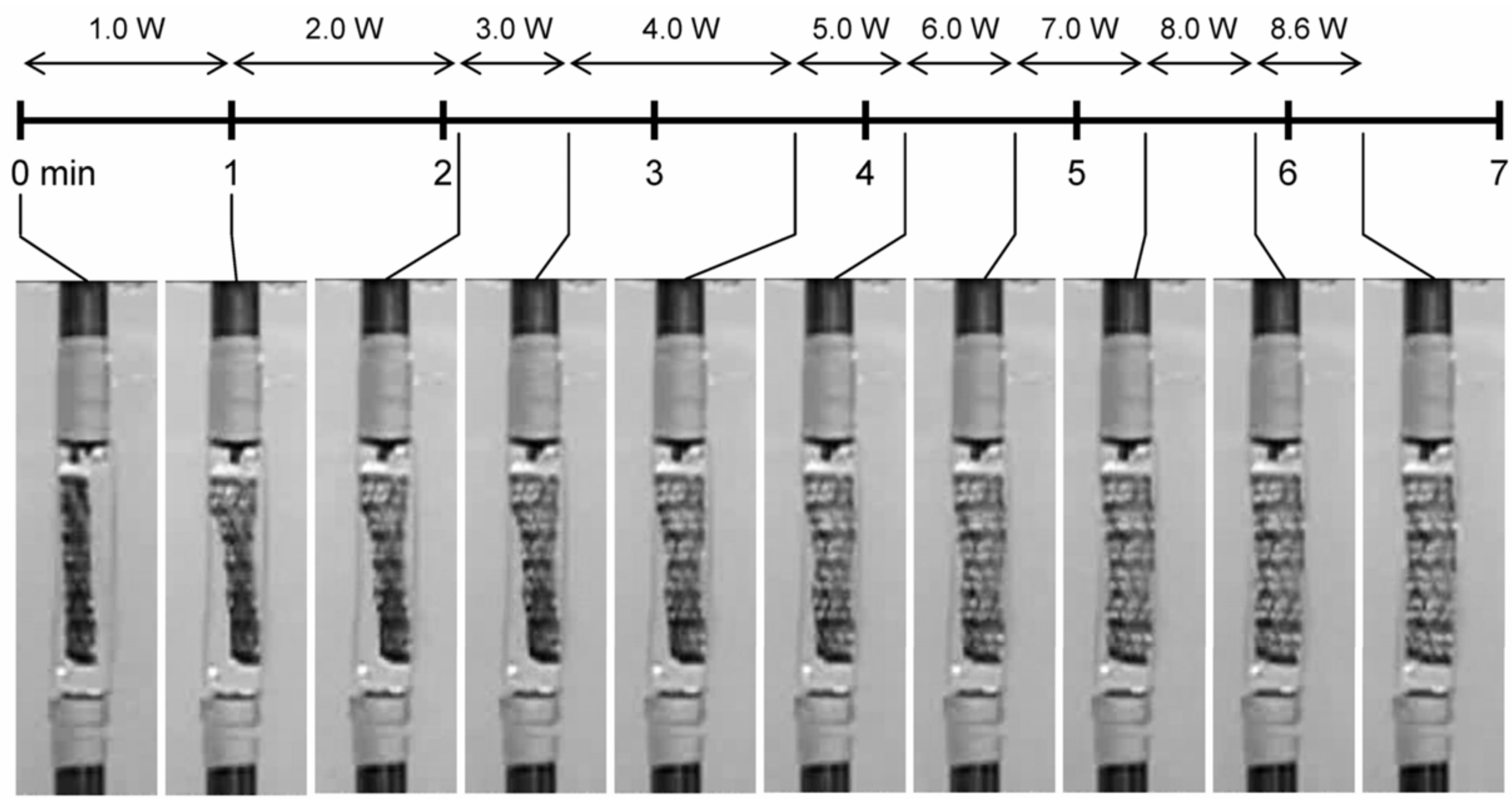
- Dip coated 4 mm dia. stainless steel pin
  - DiAPLEX, $T_g \approx 55$ °C
  - Wall thickness≈250 μm
- Pattern cut with excimer laser
- Added laser-absorbing dye
- Inserted diffuser and SMP foam cylinder
  - Center diffuser in stent lumen
  - Improve illumination uniformity
  - Reduce convective cooling
- Collapsed for catheter delivery using crimping machine with heated blades





Baer et al. *Biomed Eng Online* (submitted)

In vitro deployment of SMP vascular stent

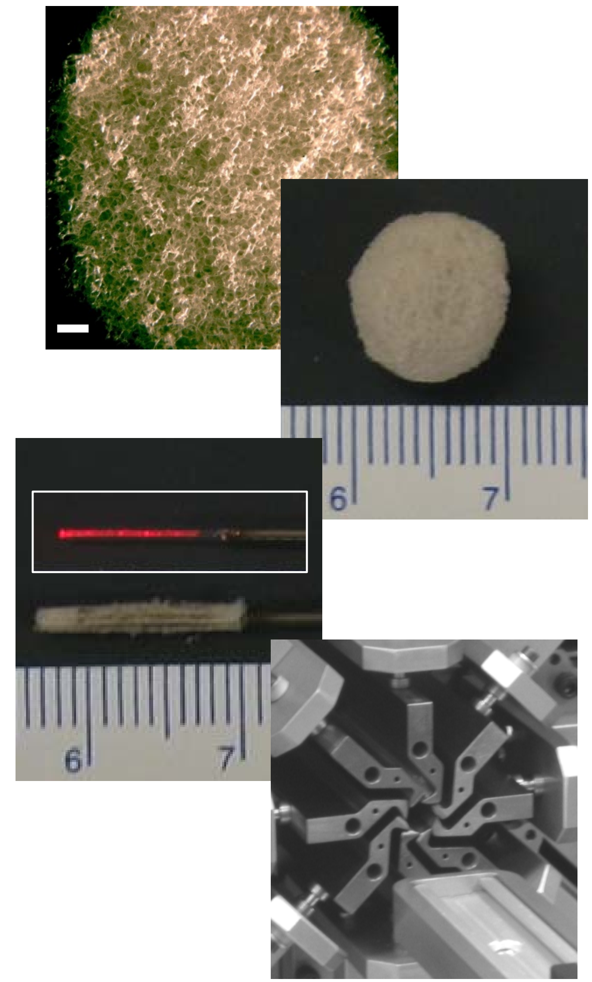


Baer et al. *Biomed Eng Online* (submitted)

- Zero flow; 37 °C water
- Only ~60% expansion when flow increased to 180 cc/min (carotid artery)

Fabrication of SMP embolic foam

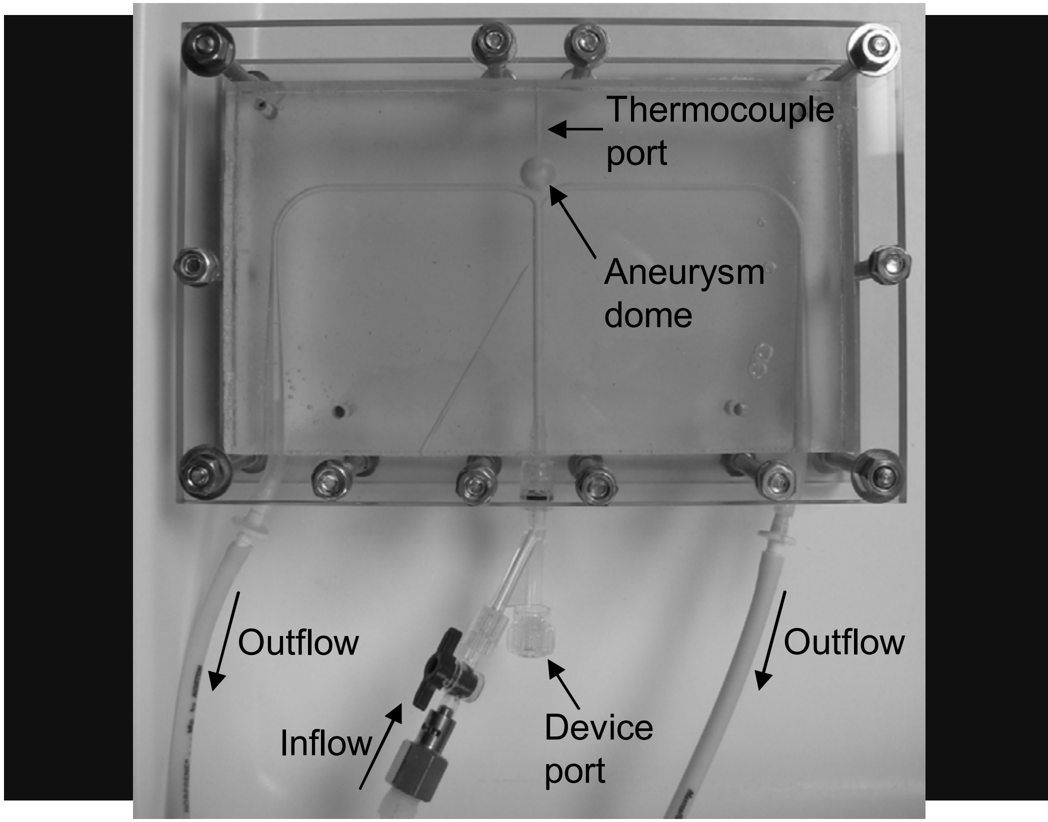
- Open-cell foam developed at LLNL
  - $T_g \approx 45$ °C; adjusted by varying monomer ratios
  - Density=0.02 g/cc;
  - ~60X volume expansion
  - Dye added during or after processing
- Collapsed over a diffuser for endovascular delivery
  - Crimping machine with heated blades



Maitland et al. *J Biomed Opt Lett* 12, 030504 (2007)

In vitro aneurysm deployment

- Two silicone elastomer halves cast around CNC-milled part
- Room temperature (21 °C) water
  - Low T_g foam would expand at body temperature (37 °C)
- Flow rates 0-148 cc/min
  - 0: blocked flow
  - 70 cc/min: basilar diastolic
  - 148 cc/min: basilar systolic



Maitland et al. *J Biomed Opt Lett* 2007

Part III

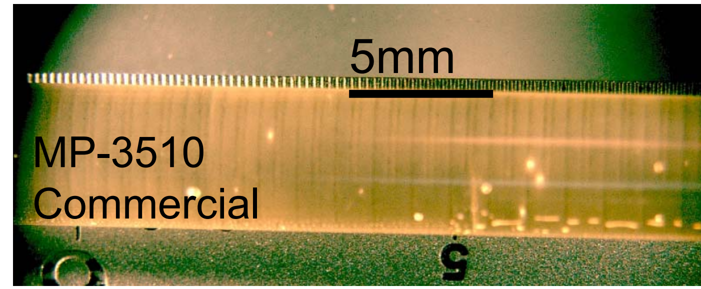
Current Directions

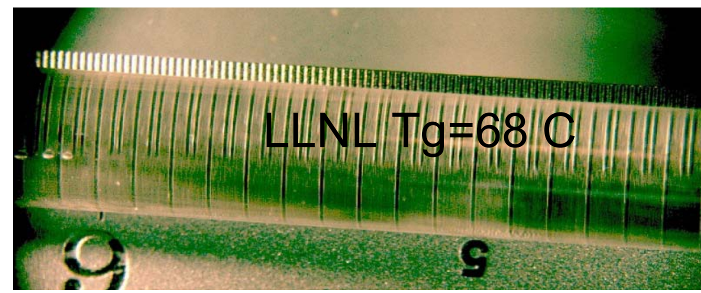
New SMPs

Courtesy of T. Wilson
Advanced Materials I, Tuesday, 11am

LLNL urethane SMPs designed for laser actuated therapeutic device use:

- Based on HDI, TMHDI, IPDI, HMDI, HPED, and TEA (urethane) chemistry.
- Amorphous thermoset polymer
- Optically clear
- Tg's from 34 to ~145 ^{o}C
- Very sharp (glass) transitions
- High recovery force
- High % shape recovery
- Aliphatic => biocompatibility
- No ester/ether links => biostable
- Use neat or as open cell foam



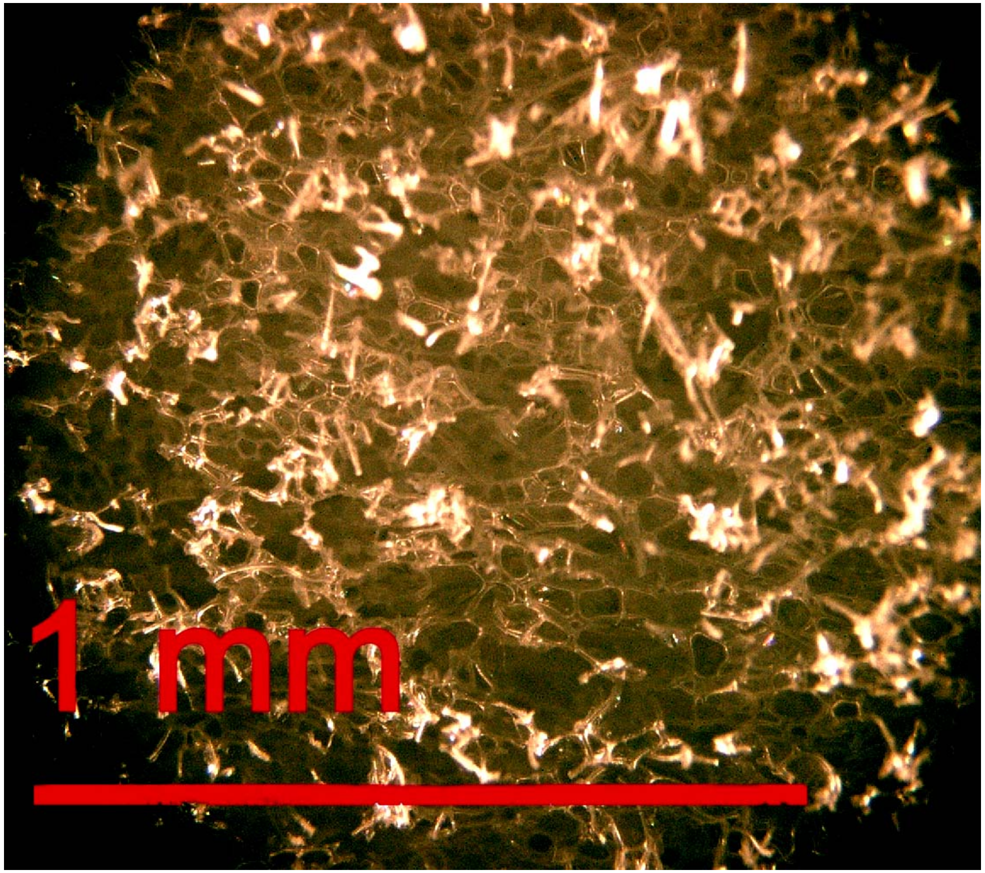


T.S. Wilson et.al., *JAPS*, **106(1**), 540, 2007.

Targeted Processing and Fabrication

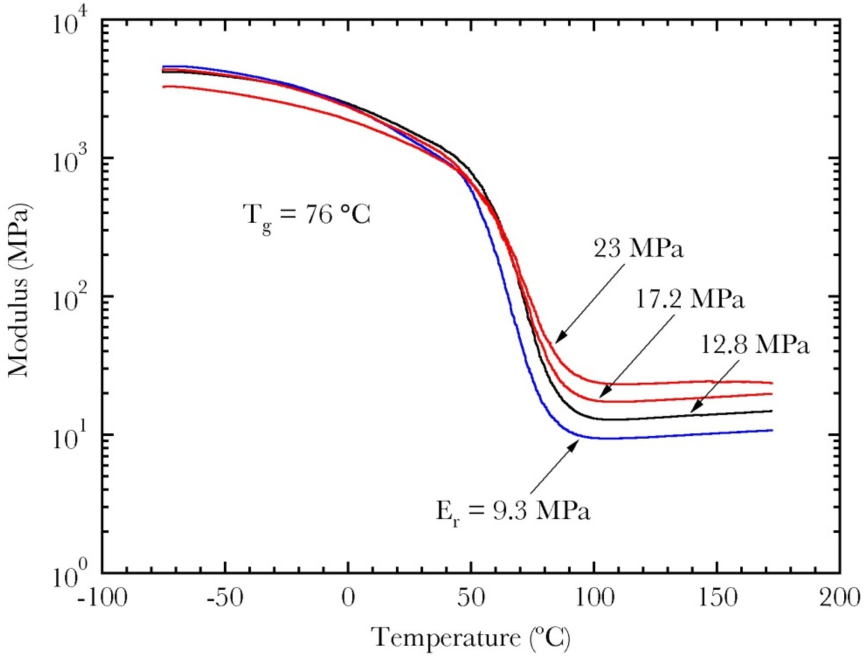
Characteristics:

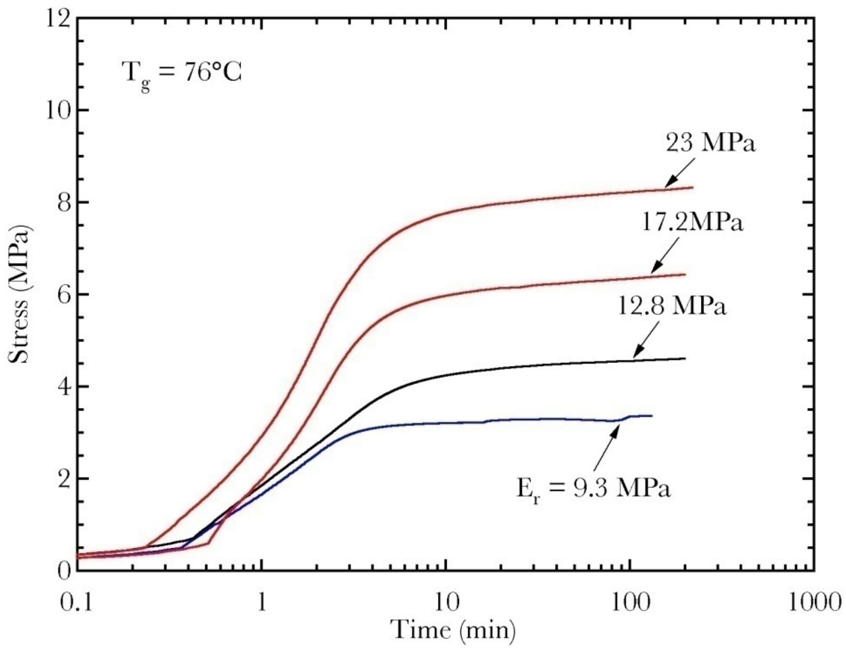
- Chemically/physically blown urethane network foams
- Highly open cell structure
- Porosities up to 98.6%
  (Volume Expansibility to ~70x)
- Tg’s from ~ 40 to 90 ^{o}C
- Composition HDI, TMHDI, HPED, and TEA
- In Vitro results suggest good biocompatibility.



Courtesy of T. Wilson

Linking Chemistry and Mechanics





Change in Chemistry to Vary Rubbery Modulus at Constant Tg

Tuned Variation in Recoverable Stress (Under Constraint) at Constant Activation Time

K. Gall and C. Yakacki: Work in Review

Predictive Modeling

Courtesy of K. Gall

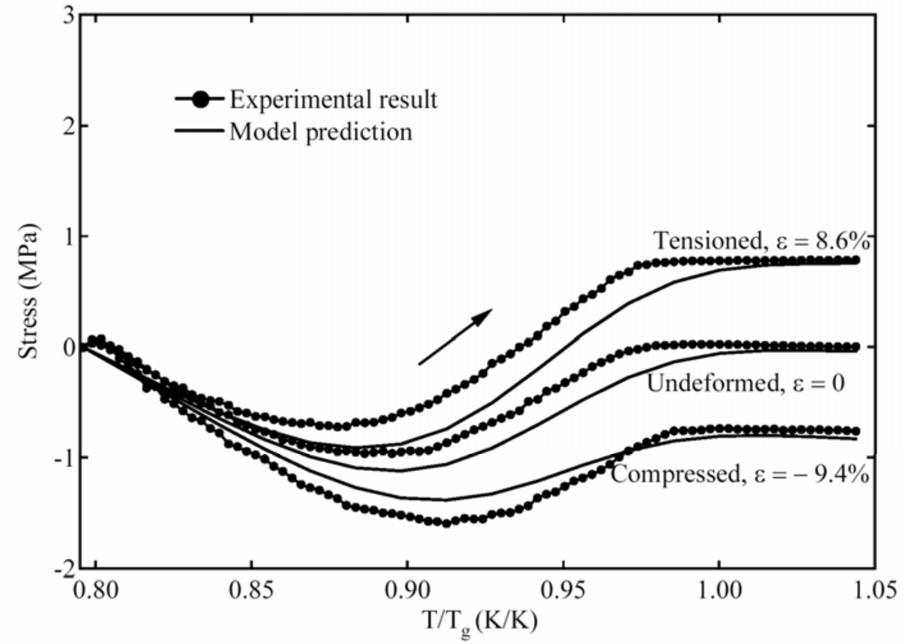
$$\sigma = \frac{\varepsilon - \varepsilon_s - \int_{T_h}^{T} \alpha \, dT}{\frac{\phi_f}{E_i} + \frac{1-\phi_f}{E_e}} = E\left(\varepsilon - \varepsilon_s - \int_{T_h}^{T} \alpha \, dT \right)$$

$$\phi_f = 1 - \frac{1}{1 + c_f (T_h - T)^n}$$

$$\frac{d\varepsilon_s}{dT} = \frac{\varepsilon - \varepsilon_s - \int_{T_h}^{T} \alpha \, dT}{E_e \left(\frac{\phi_f}{E_i} + \frac{1-\phi_f}{E_e} \right)} \left(\frac{d\phi_f}{dT} \right)$$

$$E_i = \text{constant} \qquad E_e = 3NkT$$

Constitutive Framework

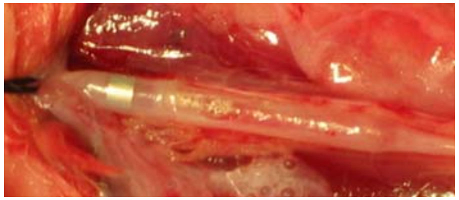


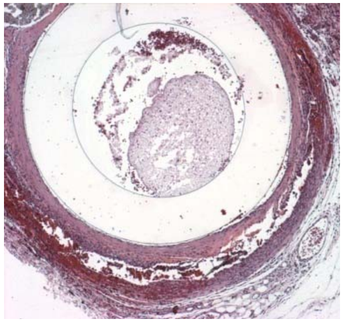
Constrained Stress Prediction

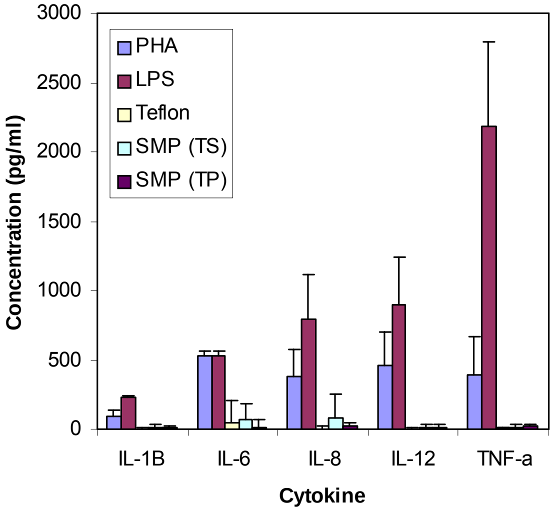
Y. Liu, K. Gall, M. L. Dunn, A. R. Greenberg, and J. Diani (2006) Thermomechanics of Shape Memory Polymers: Uniaxial Experiments and Constitutive Model. *International Journal of Plasticity*, vol. 22, pp. 279-313.

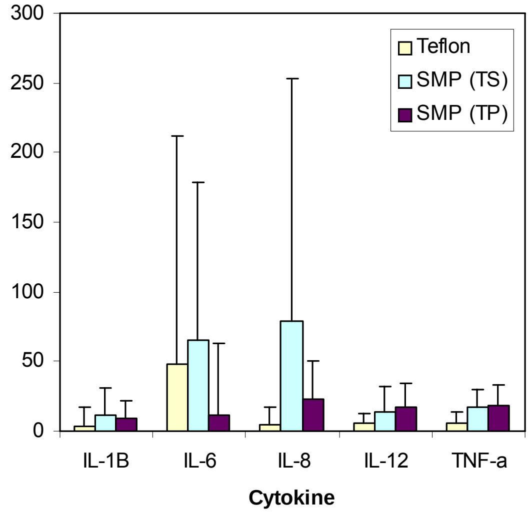
SMP biocompatibility

- In vitro: Diaplex and LLNL neat and foam - negative activation of human platelets, cytokines, t-cells, negative toxicity (Cabanlit et al. Macromol Biosci 2007).
- In vivo: negative inflammatory or adverse thrombogenic response [foams (Metcalf et al., Biomat 2003), stents (in prep)]



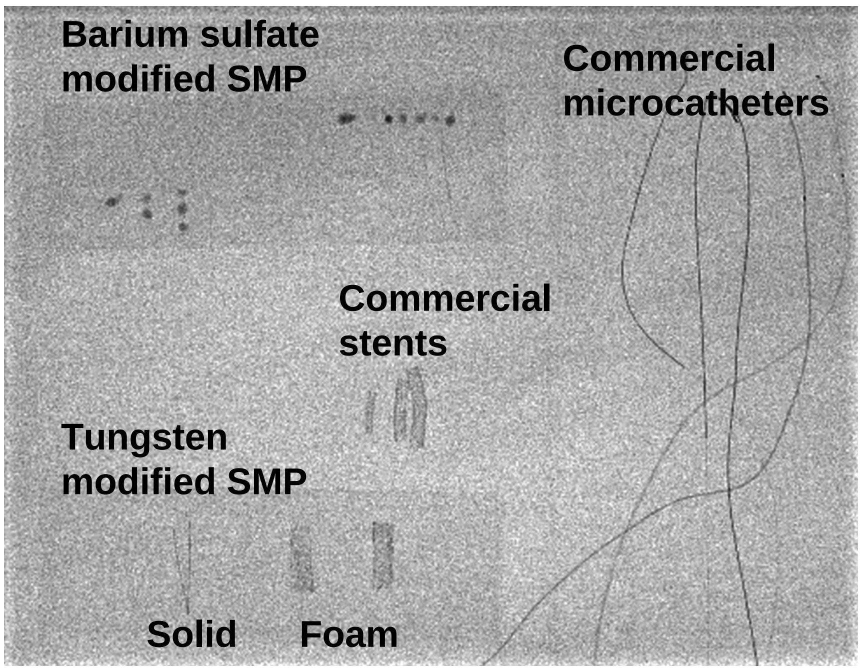


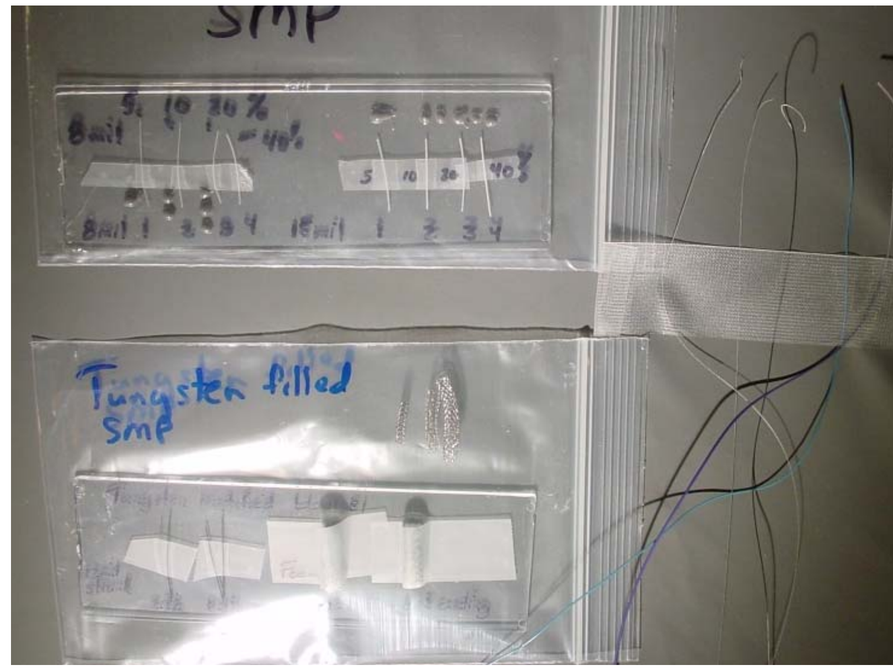




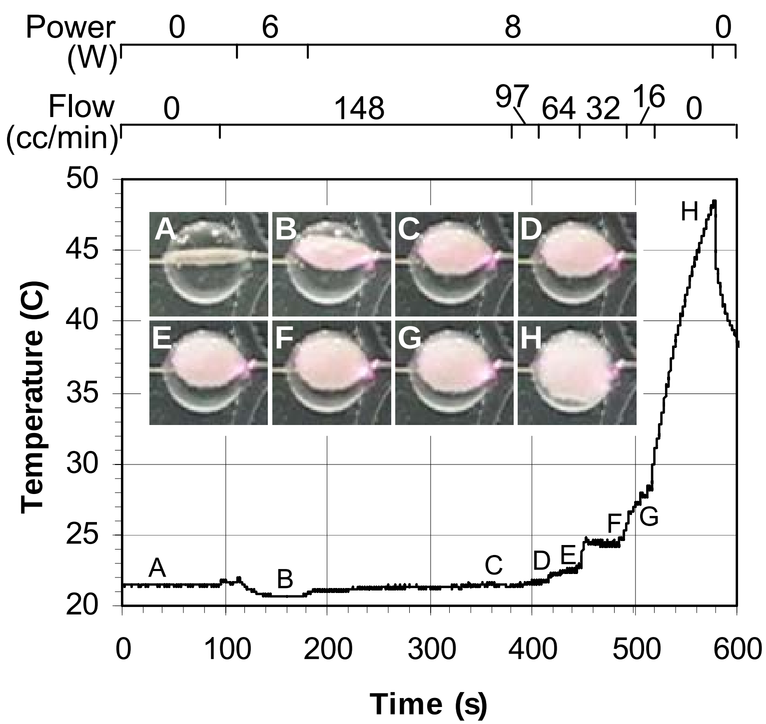
Cabanlit et al. *Macromol Biosci* 7, 48-55 (2007)

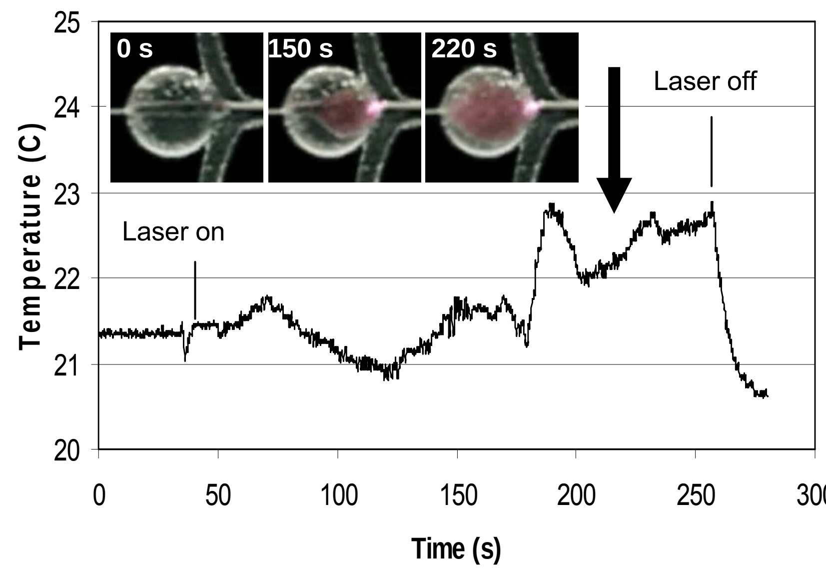
Radiopacity of SMP composites





Device-body interactions: in vitro deployment of SMP embolic foam



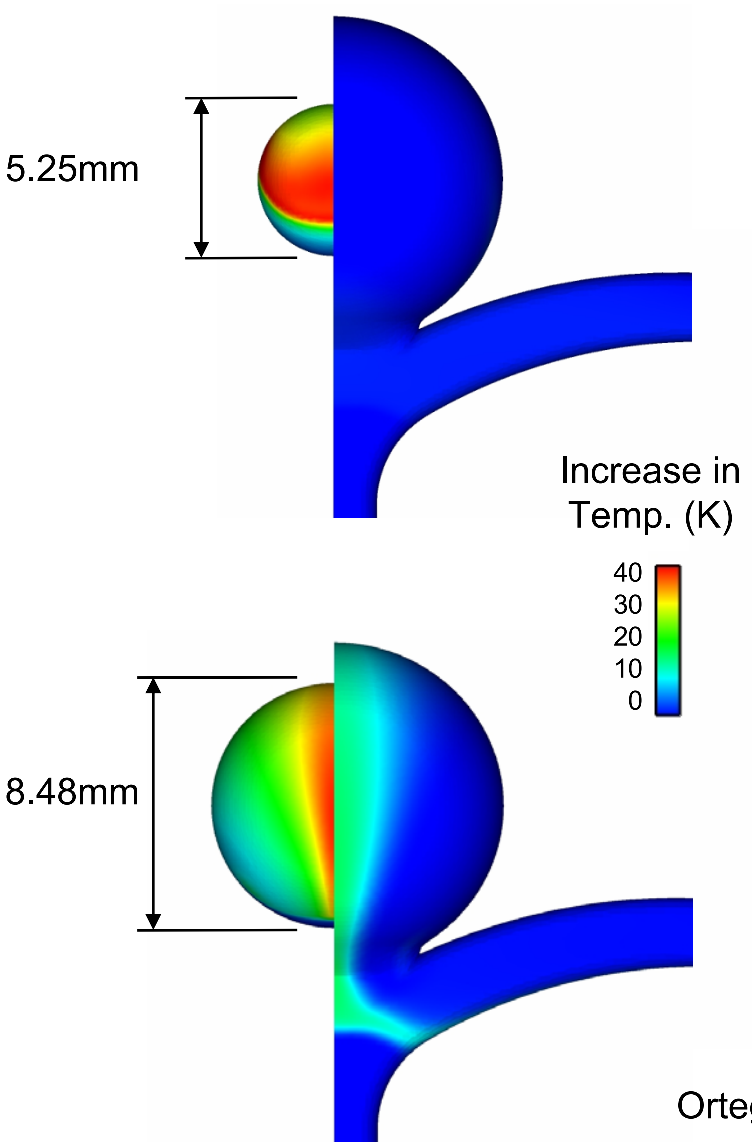


- With flow, convective cooling prevented full expansion
- With zero flow, full expansion in 60 s with $\Delta T \approx 30$ °C (not shown)

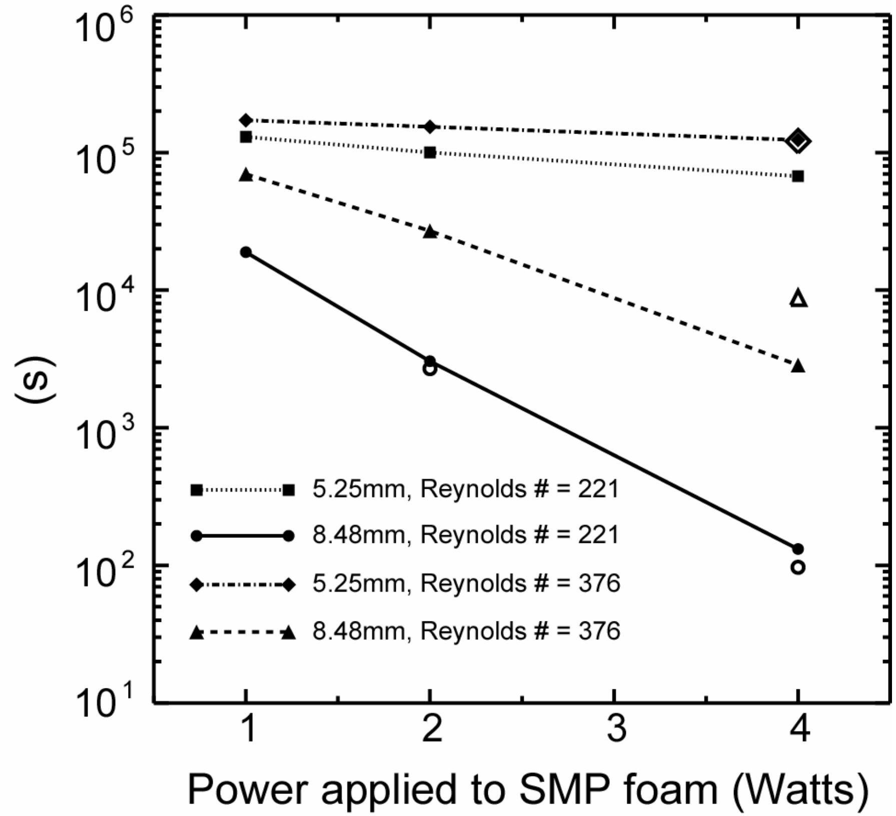
- Extra dye added to overcome convective cooling
- Laser power slowly ramped to 8.6 W over 3 min
- At 70 cc/min, full expansion in 3 min with $\Delta T < 2$ °C

Maitland et al. *J Biomed Opt Lett* 12, 030504 (2007)

CFD provides an estimate of thermal damage resulting from the heated SMP foam



Time scale for thermal tissue damage to the aneurysm



Ortega et al. *Ann Biomed Eng* (2007)

Summary

- The application of SMP to Medical Devices in its infancy
  - ~12 academic groups publishing medical SMP research
  - 6+ companies pursuing SMP medical devices
  - 2+ companies selling SMP
- Significant commercial cruxes remain – aging, fabrication, sterilization, long-term toxicity
- Our team will continue to work on interventional applications with Stroke focus
  - Emphasis on device-body interactions (physics, biocompatibility, image-guided delivery)
  - Document commercially relevant topics
  - Pre-clinical studies
  - Engineered bulk and surface chemistry for biological applications

Acknowledgments

Financial support

- National Science Foundation Center for Biophotonics (CBST). CBST, an NSF Science and Technology Center, is managed by the University of California, Davis, under Cooperative Agreement No. PHY 0120999.
- NIH National Institute of Biomedical Imaging and Bioengineering Grant R01EB000462 (BRP)
- LLNL Laboratory Directed Research and Development Grants 04-LW-054 and 04-ERD-093

Co-investigators

LLNL:
Ward Small
Tom Wilson
Bill Benett
Jane Bearinger
Wayne Jensen
Jason Ortega
Julie Herberg
Erica Gersjing
Jennifer Rodriguez
Melodie Metzger

UC Davis:
Jon Hartman
Judy Van de Water
Scott Simon
Robert Gunther
Bill Ferrier
Ted Wun
John Brock
Maricel Cabanlit
Eric Gershwin
Geraldine Baer

UC Berkeley:
Omer Savas
Wil Tsai

UCSF:
David Saloner

This work was performed under the auspices of the U.S. Department of Energy by University of California, Lawrence Livermore National Laboratory under Contract W-7405-ENG-48.