Developing Methods for Accelerated in-vitro Aging and Testing Flexural Stiffness of Gynecological Surgical Mesh Implants

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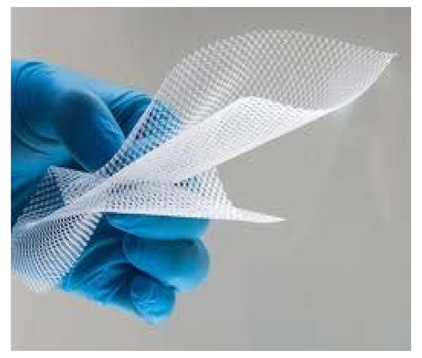
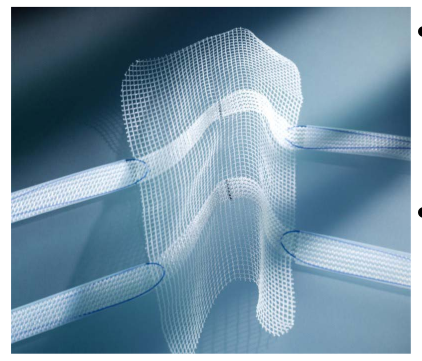
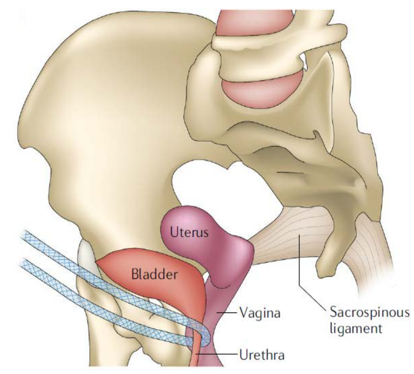
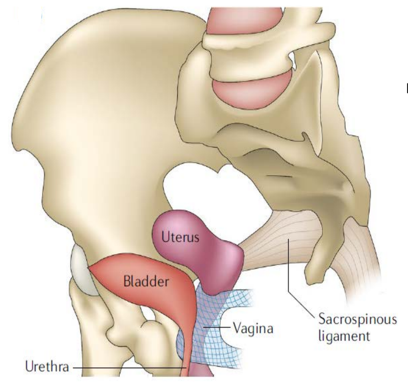
Introduction

Commercial Surgical Mesh Examples



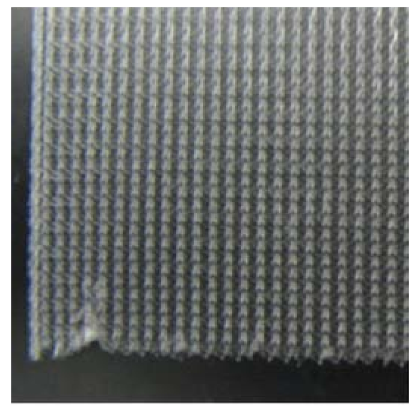
Transvaginal mesh for SUI[1]



Transvaginal mesh for POP[1]

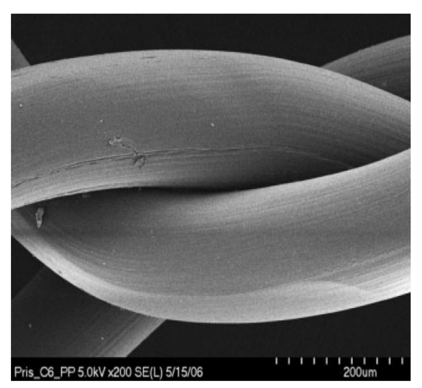
- Surgical mesh are porous polymer sheets used to provide additional support to weakened or damaged tissue or to repair or reconstruct anatomical defects.
- Most mesh-related surgeries in U.S. are performed for hernia repair (~ 1 million/per year[1]) followed by pelvic floor reconstructive surgeries for conditions such as pelvic organ prolapse (POP) (~300,000 in 2010[2]) and stress urinary incontinence (SUI) (~250,000 in 2010[2]).
- Several materials have been used in surgical meshes, most common is polypropylene (PP) because of lower erosion rates, better mechanical properties, a lower inflammatory and immune response, and better integration within tissue than meshes made of other synthetic materials.

Motivation



Pristine mesh[2]

3-yr explanted mesh[2]



Pristine mesh SEM[3]

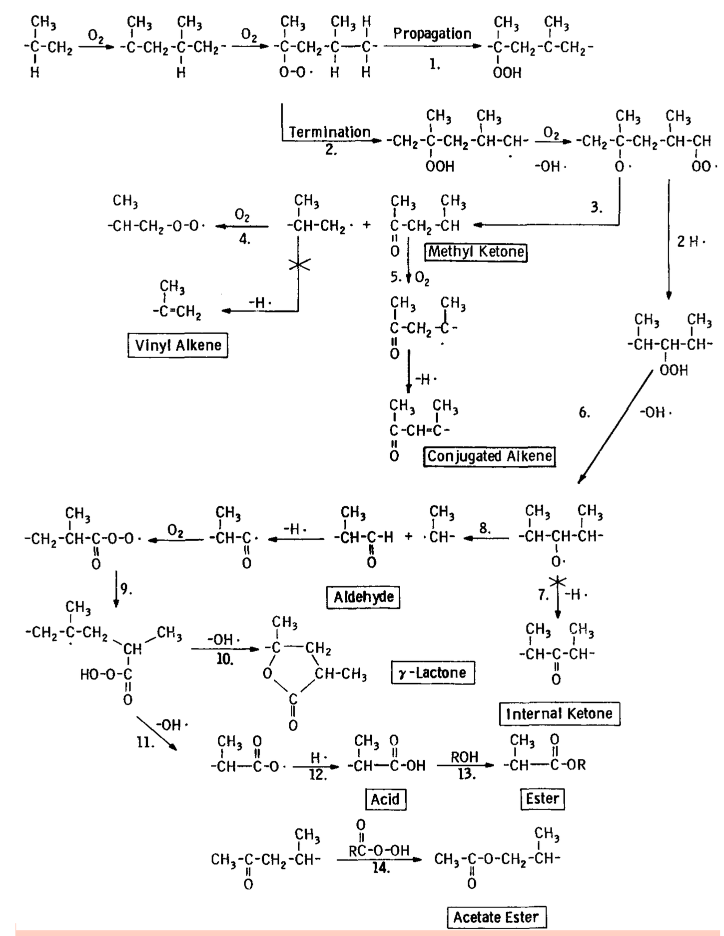
Explanted mesh SEM[3]

- PP mesh had subjective success rates of up to 92% for treating hernia, SUI, and POP when implanted transabdominally[3]; mesh related complication rates up to 42% were reported for transvaginal implantation for POP repair (TVM)[4].
- PP mesh can cause chronic or prolonged inflammatory reaction leading to oxidative stress due to an imbalance between the production of oxidants, like reactive oxygen species (ROS), nitrogen species (RNS), and lipid peroxidation (LPO) products, and the antioxidant capacity of cells or tissues.
- PP mesh erosion has been reported in 10.3% cases when used for POP[5] compared to 2.2% cases when used for SUI.[6] Pieces of implanted mesh have been found to have eroded into the urinary bladder, rectum, vaginal wall and other pelvic organs which results in lifelong pain and severe discomfort for the patients.

Identified Gaps

- No standardized methods exist for accelerated testing of long-term biostability of surgical mesh in a physiological environment.
- Surgical mesh used for POP are subjected to multiaxial biomechanical stresses. However, predominantly uniaxial tensile tests are reported to characterize mechanical properties of mesh. Test methods for mechanical characterization should be developed to resemble the physiological conditions of the implanted surgical mesh.

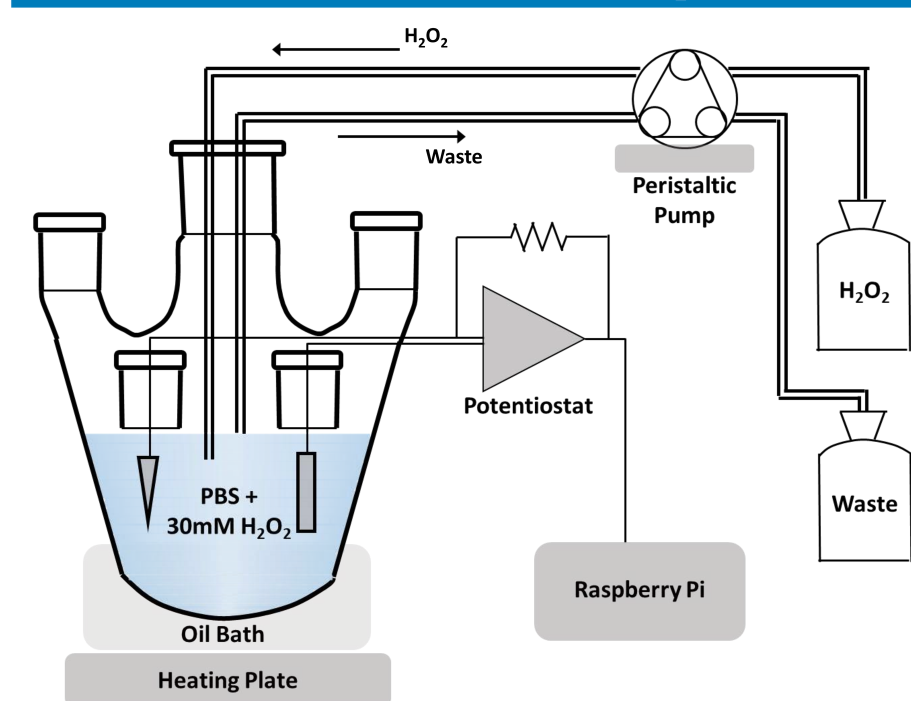
Polypropylene Oxidation



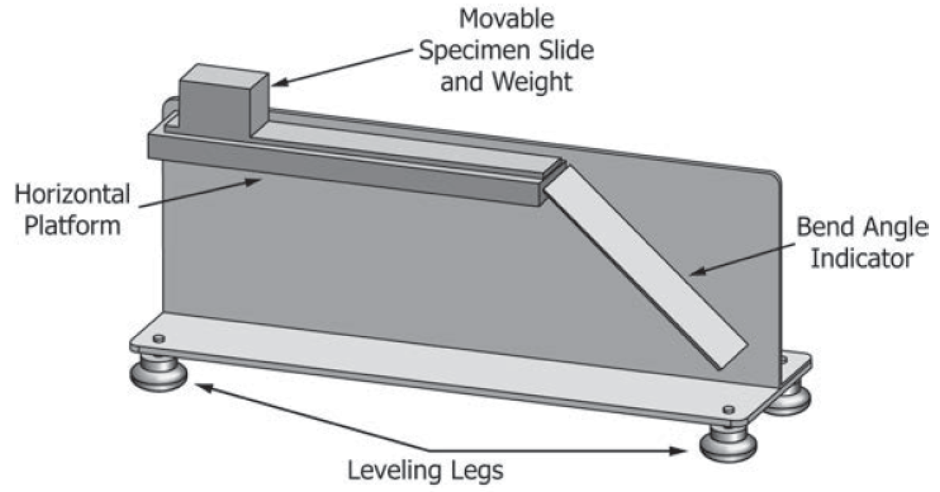
Polypropylene Oxidation Scheme

- PP is prone to oxidation which can lead to fiber cracking, surface damage, mass loss, change in mechanical properties, pore area shrinkage, particulate debris, mesh erosion, and overall implant failure.
- PP oxidation usually occurs at the tertiary carbon centers leading to formation of hydroperoxides. The decomposition of hydroperoxides results in chain scission, introduction of functional groups into the polymer chains, and formation of volatile products.
- 50% of oxidation products are volatile by-products such as water, acetone, acetaldehyde, formaldehyde, methane, ethane, propane, propylene, ethylene, etc. (total 49 identified[1]) and the other 50% are solids in the form of functional groups such as acids, ketones, aldehydes, esters, and y-lactones on PP chains.

Experiment Design



Automated Reactive Accelerated Aging (aRAA) Setup



Cantilever Test Apparatus for Flexural Rigidity Measurement

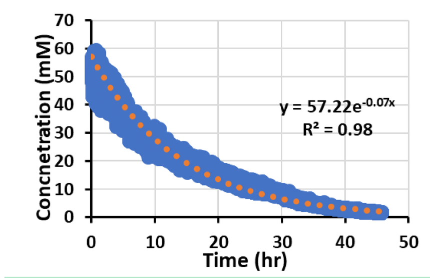
aRAA:

- Mesh samples (25mm x 200mm) were immersed in 150 ml of PBS solution with 30mM or 100mM hydrogen peroxide (H_2O_2) at 85°C.
- H_2O_2 concentration was maintained using a peristaltic pump to supply fresh concentrated H_2O_2 and remove excess solution from the flask.
- H_2O_2 concentration was monitored using a two-electrode setup which was connected to a potentiostat that applies cyclic voltages and records the corresponding current.
- The peristaltic pump and the potentiostat are controlled by a Raspberry Pi device and a IoT relay.

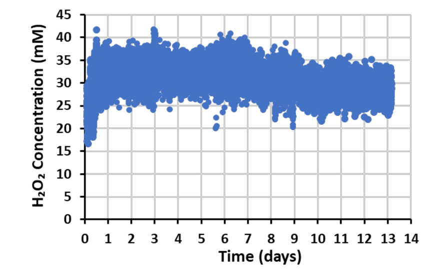
Flexural stiffness testing:

- Mesh samples of various weights (g/cm^2) were tested using the cantilever test apparatus to determine their flexural rigidity (N-m).
- The samples were tested in the machine and cross-machine cut directions, and surface orientation effects were also measured.

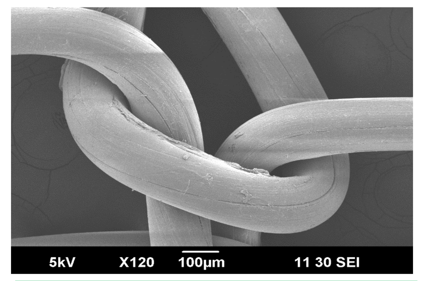
Preliminary Results



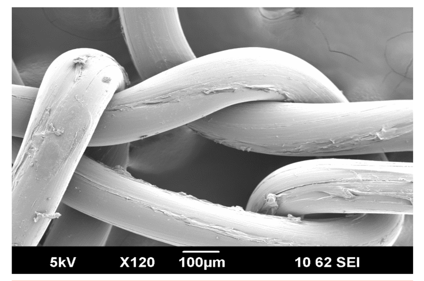
H_2O_2 decomposition



Steady H_2O_2 conc.

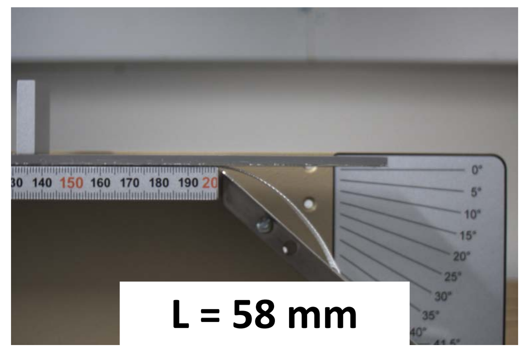


Pristine Mesh SEM

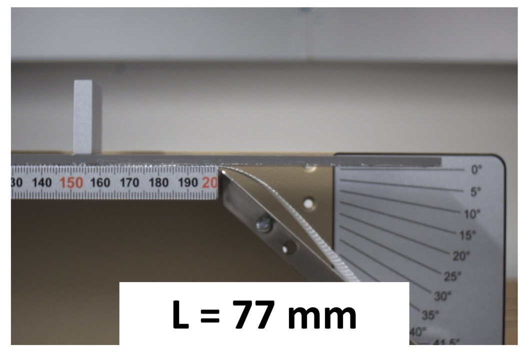


1-week RAA SEM

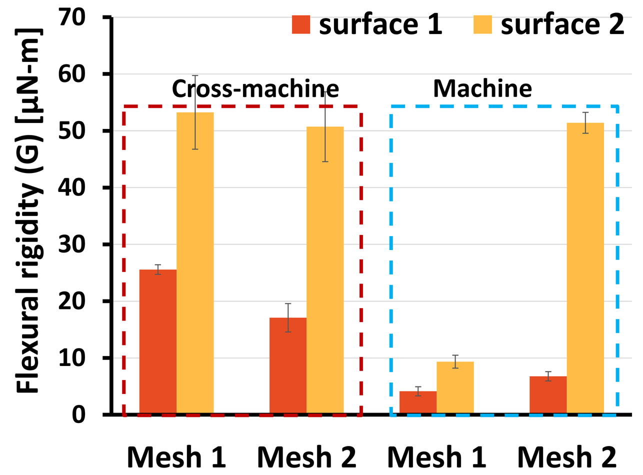
- H_2O_2 had a half life ($t_{1/2}$) of 9.6 ± 0.4 hr. and first-order decomposition constant (k) of 0.072216 hr^{-1}. Steady H_2O_2 concentration of 30mM and 100mM were maintained for at least two weeks.
- Samples oxidized for 2 weeks at 30mM did not have an observable effect on the surface. However, samples oxidized for 1 week at 100mM showed increased crack propagation and flaking on the mesh surface.



Overhang Length – Top Surface



Overhang Length – Bottom Surface



Flexural Rigidity

- Mesh 1 of weight 9.6 g/cm² had significant differences in flexural rigidity when compared in the machine and cross-machine directions, and for both surface orientations.
- Mesh 2 of weight 6.3 g/cm² had no significant differences in flexural rigidity when compared in the machine and cross-machine directions, however the rigidity varied significantly between the top and bottom surface.

Preliminary Conclusions

- H2O2 based reactive accelerated aging (aRAA) method may be used for testing long-term oxidative stability of polypropylene surgical mesh. The method allows for continuous monitoring and maintaining steady concentration of oxidative species like H_2O_2 at high temperatures.
- Surface damage was observed using SEM after 1 week at 85°C and 100 mM H_2O_2.
- Experiments with samples immersed for longer times are on-ongoing. Addition of cobalt chloride ($CoCl_2$) as a catalyst to further accelerate the oxidative degradation is being tested.

References & Acknowledgements

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