Among the first polyurethanes used in device applications were hydrolytically-unstable thermoplastics or two-component systems based on poly(adipate)ester soft segments. These materials degraded in vivo causing device failure. Even before 1970 polyether-based urethanes incorporating polytetramethylene oxide (PTMO) soft segments were identified as being inherently stable to hydrolysis and for having excellent flex life. For many years solvent-cast, segmented polyether-urethanes with polyurea hard segments (and their thermoplastic analogues with urethane hard segments) remained the preferred materials for chronic implants. This was especially true in applications requiring continuous flexing, e.g., in pacing leads and in cardiac assist devices like intraaortic balloons, VADs and artificial hearts. Many of the polymers in clinical use were originally developed for industrial applications and then adopted as biomaterials ‘as is’, or after some purification. One polymer developed specifically as a biomaterial was Avcothane-51 (a.k.a. Cardiothane-51) a hybrid/pseudo-interpenetrating network of linear polyetherurethane modified with silicone that crosslinked after device fabrication.

Since the late 1970s we have been developing and manufacturing segmented and thermoplastic polyurethane multipolymers with two or more soft segments combined along the polymer backbone. The use of more than one soft segment allows polymer properties to be optimized by controlling the concentration of each soft segments, and the total soft-segment to hard-segment ratio. One of our early multipolymers used the thermodynamically compatible polyalkyleneoxides PTMO and polyethylenoxide (PEO). The resulting series of polymers has a huge range of permeabilities to water, gases and solutes depending on the ratio of hydrophilic PEO to hydrophobic PTMO. These are currently used as membranes and in occlusive dressings. As films or coatings they provide high moisture vapor permeability combined with liquid and microbial barrier properties.

Some very useful polyurethane multipolymers are based on poyalkyleneoxides (e.g. PTMO) and polydimethylsiloxane. We first developed these in the early 1980s (US 4,675,361) and used them in VADs and vascular grafts. More recently we have studied improved polymers with mixed soft-segments, e.g. PurSil™ thermoplastic silicone-urethane (TSPU). As the silicone content of the soft segment is increased, biostability increases to a maximum (at < 100% silicone), and strength decreases monotonically. This is a truly synergistic combination of reactants that can be optimized to provide high levels of biostability and toughness for demanding in vivo applications. A variation of this system uses polyhexamethylene carbonate in place of PTMO to further increase toughness, and to avoid the metal-oxide-induced oxidative instability of polyethers in certain applications. This silicone-polycarbonate-urethane, is known commercially as CarboSil® TSPU.
We recently built a continuous reactor to synthesize biomedical polyurethanes, and multipolymers including silicone-polyurethane copolymers. The reactor includes: holding tanks for reactants, metering pumps with flow controllers, an instrumented extruder with screen changer, a diverter valve and an underwater pelletizer (see photo). Pellet collection takes place in a cleanroom after dewatering and drying of the pellet slurry. Optionally, the rail-mounted extruder can be fitted with a multi-strand extrusion die with air cooling. Polymer output ranges from 20 to 100 lb per hour, depending on reaction kinetics as determined by pH, catalyst level, temperature, etc. This output range is ‘production-scale’ for many polymers used in chronic implants. Current applications include pacemaker and neural stimulation leads, cardiac assist devices, dynamic spinal fixation, prosthetic spinal discs, hip joints, central venous catheters, and other devices and prostheses that must function within the body for multi-year periods.

The optimization of polymeric biomaterials for (chronic) implantation requires consideration of both bulk and surface properties. Today we use, a polyurethane backbone with mixed soft segments and a single hard segment chemistry to tailor bulk properties. We control surface properties via self-assembling Surface-Modifying Endgroups (SME) incorporated during synthesis. The continuous reactor is well suited for polymer optimization when run in development-mode, during which designed experiments can be performed to vary stoichiometry, backbone chemistry and endgroup chemistry and concentration. A single day of experimentation can yield up to ten 10-kg samples for characterization and/or prototype device fabrication.

Polymers that are modified with SMEs may demonstrate improved biological interactions relative to unmodified homologues. (This can lead to improved device safety or efficacy.) This is true even when the modification affects only the outer few molecular monolayers. Highly surface-specific analytical methods are needed to characterize polymers with SMEs, and other biomedical materials as well. Since 1995 we have promoted the use of the non-linear optical technique known as Sum Frequency Generation Vibrational Spectroscopy (SFG). By combining SFG with the development and manufacturing capability of our continuous reactor we are attempting to streamline the systematic development of biomedical polymers for a wide range of new devices and prostheses currently under development.

References:
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