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New Multidetector Solution Could Lead to Safer Alternatives to Faulty Silicone Breast Implants

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Combining viscometry and light scattering technology with a refractive index detector enables development and characterization of alternative materials to silicone breast implants.

According to the American Society of Plastic Surgeons National Clearinghouse of Plastic Surgery Procedural Statistics, there were 296,203 breast augmentation procedures and 93,083 breast reconstruction procedures performed in the U.S. in 2010. Approximately half of these procedures used saline-filled implants and half used silicone gel-filled implants. However, concerns have been raised as silicone gel-filled implants have been associated with a number of issues including capsular contracture, gel bleed, implant rupture and infection. Saline-filled implants have lower rupture rates but are perceived as inferior in "naturalness" when compared with silicon gel-filled implants. These prevalent issues led to the need for material scientists and medical doctors to work together to develop alternative materials based on new nanotechnology.

U.S. regulations

In November 2006, the U.S. Food and Drug Administration (FDA) approved two silicone gel-filled breast implants for increasing breast size in women age 22 or older, and for reconstruction after breast cancer surgery or other medical issues in all women. The implants are also approved for revision surgeries, which correct or improve results of original augmentation or reconstruction surgery.

As a condition of approval, the FDA required each manufacturer to conduct post-approval studies to characterize the long-term performance and safety of the devices.

In June 2011, the FDA published a report that includes preliminary safety data from these studies, as well as other safety information from recent scientific publications and adverse events reported to the FDA. According to the report, the FDA continues to support the safety and effectiveness of these implants when used as intended, but states that women should be thoroughly informed about and fully understand the risks before considering undergoing surgery. Studies to date do not indicate that silicone gel-filled breast implants cause breast cancer, reproductive problems, or connective tissue disease. However, no study has been large or long enough to completely rule out these and other rare complications. As a consequence, there is a need for safer alternatives to traditional silicone gel-filled breast implants.

The promise of alternative biomaterials

Similar to almost all other soft materials used in the construction of biomedical devices in clinical practice, silicone elastomer nanocomposites used in breast implants are derived from products originally developed for industrial use. The most critical problem with all synthetic biomaterials is adverse tissue reaction. The ultimate challenge is to design and produce a suitable biomaterial for use in breast implants that will demonstrate mechanical similarity to native breast tissue, while also being biocompatible, sterilizable, mechanically and physically robust, and easily processible.

The University of Akron's Department of Chemical and Biomolecular Engineering is part of an interdisciplinary group that is pursuing research aimed at reducing/eliminating capsular contracture associated with breast

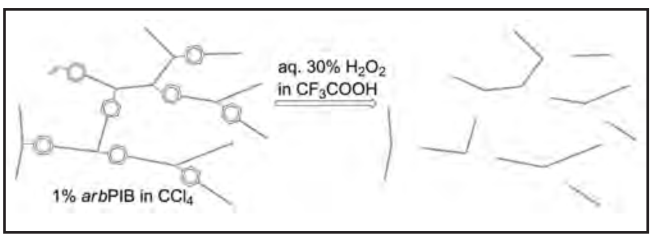

Fig. 1 — *Aromatic link destruction method.*

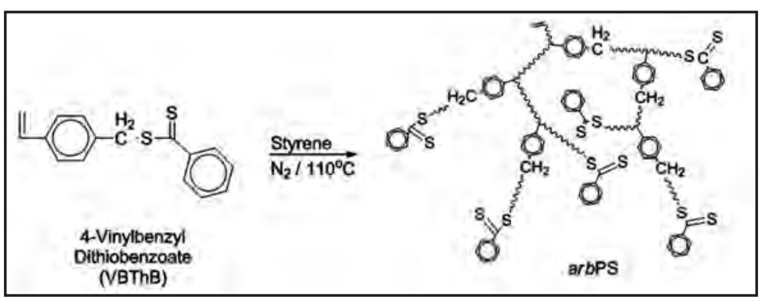

Fig. 2 — *One-pot synthesis of arbPS. Fragmentation of VBThB (4-vinylbenzyl dithiobenzoate) results in the formation of an active radical, which can initiate polymerization.*

implants to help women in need. Material science and nanotechnology are a key element of this, supported by top-class instrumentation.

Branched polymers are intrinsic to finding an alternative to silicone breast implants. This type of polymer is of considerable interest to both academic researchers and industry due to the unique combination of properties compared with their linear counterparts. While silicone breast implants can lead to rupture, gel bleed, and sagging, branched polymers provide better shape retention than any alternative substance.

However, branched-polymer analysis poses a number of challenges. In principle, inimer (initiator-monomer) polymerizations lead to simultaneous chain growth and branching, resulting in multiple distributions of branched molecules, with more branches in the high molecular weight fractions. The selective link destruction technique used in the analysis of arborescent (tree-like) polyisobutylene (arbPIB) cannot be extended to arborescent polystyrenes (arbPS) made by RAFT (reversible addition fragmentation chain transfer) polymerization (Fig. 1). This renders branching characterization very difficult.

This article highlights the comparative architectural analysis of arbPSs and arbPIBs using high resolution multidetection size exclusion chromatography (SEC), refractive index (RI), multiangle light scattering (MALS), quasielastic light scattering (QELS), and viscometry (VIS) detectors.

New multidetector technology

Traditionally, column calibration-based SEC was used to analyze branched polymers, even though this technique was indirect, at best. Furthermore, when SEC technology is used alone, it does not offer the ability to distinguish branched polymers from linear polymers as the technique separates by size and not shape. As a result, University of Akron researchers developed a multidetector light scattering solution to provide accurate, absolute characterization of separated macromolecules.

They are developing nanostructured drug-eluting biomaterials through the integration of four-platform technologies: (1) macromolecular engineering to precision synthesize biocompatible polymers and produce high-performance bionanocomposites, (2) electrospinning technology to provide nanotextured implant surfaces with drug-eluting nanofiber coatings, (3) design and synthesis of targeted nanodevices with therapeutic and diagnostic (theranostic) capabilities, and (4) in vitro/in vivo biocompatibility, safety and efficacy testing.

Specifically, the multidetector technology system is a combination of six gel permeation chromatography (GPC) columns (Styragel, Waters), a viscometer (ViscoStar, Wyatt Technology), an RI detector (Optilab DSP, Wyatt Technology) thermostatted at 40°C, an 18-angle multiangle light scattering (MALS) detector (DAWN EOS, Wyatt Technology), and a quasielastic light scattering (QELS) detector (Wyatt Technology) positioned at the 90° angular location on the DAWN read head.

Application

Experimental results demonstrate that the new high-resolution SEC system equipped with six GPC columns and five detectors provides an ideal solution for studying branching, because the aromatic branch points can selectively be cleaved without affecting PIB chains (Fig. 2). Application of the new technology enabled researchers to separate the effects of branching and molecular weight distribution experimentally for the first time. The six GPC columns demonstrated excellent resolution and successfully correlated bulk viscosity data with molecular weight (M_w) data, which previously was not possible using two mixed columns. Additionally, the system's two concentration detectors (RI

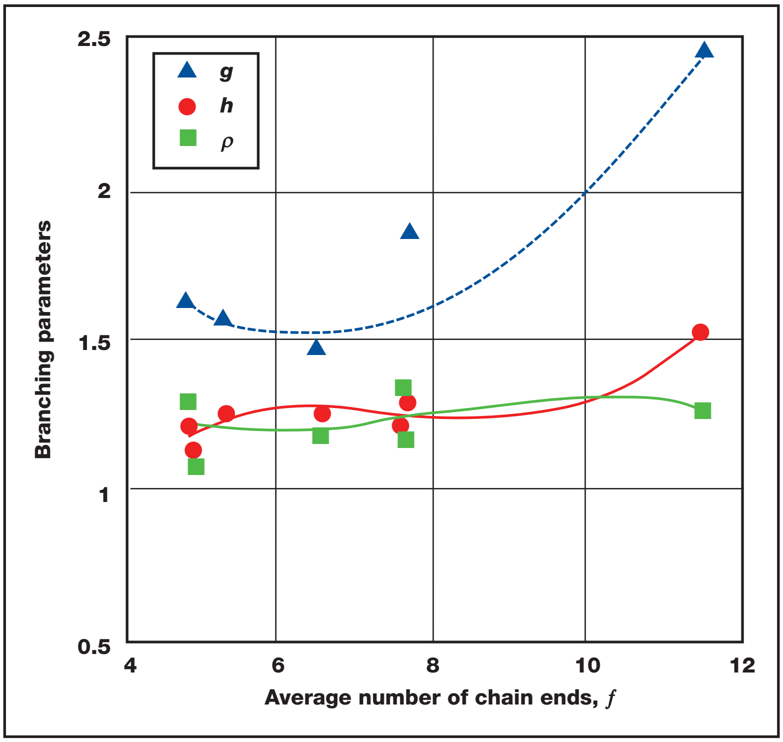

Fig. 3 — *Branching parameters g, h, and ρ as a function of f for arbPIBs, calculated as B + 2.*

and UV) facilitated measurement of sample concentration and concentration of species that absorb UV light.

Five different detectors allowed researchers to determine different parameters related to the size of the polymers. The MALS detector readily provided absolute molecular weight (M_w) and radius of gyration ($R_{g,z}$) data. This detector is essential for branched polymers, because calibration curves are unavailable for M_w determination, while added complexity is introduced if branching is not uniform. The viscosity detector allowed determination of the hydrodynamic radius ($R_{h,g}$) and the dilute solution viscosity of the polymers, which are useful parameters for branching analysis. Finally, the QELS detector yielded R_h data derived from the diffusion coefficient.

Scientists measured the R_g and R_h of linear PIB standards with low polydispersities, constructed radii–M_w plots, and computed *g*, *h*, and *ρ* for the arbPIB samples. Plots of *g*, *h*, and *ρ* as a function of the average number of chain ends (*f*), calculated as B + 2, are shown in Figure 3.

Overall, data from the high resolution SEC system were used to obtain parameters that provide insight into polymer architectures. A new preliminary prediction based on mean field theory is currently under development to describe the nature of polymers synthesized using inimer-type polymerization.

Conclusion

New multidetector nanotechnology developed by the University of Akron's Department of Chemical and Biomolecular Engineering holds promise for safer alternatives to silicone gel-filled breast implants. This is a significant development as silicone gel-filled breast implants are associated with a number of shortcomings. Researchers believe that encapsulation and local delivery of cancer drugs from nanofiber coatings on the proposed novel breast prostheses with a specificity to target receptors on cancer cells is a unique, innovative approach to address the undesirable side effects associated with current chemotherapy. The new technology also has potential in early diagnosis and imaging of breast cancer.

Wyatt Technology's innovative SEC detectors enabled the University of Akron to win GE Healthymagination Breast Cancer Challenge along with four other companies. ❍

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