Limitations of Predicting *In Vivo* Biostability of Polydimethylsiloxane Based Polyurethanes using Time Temperature Superposition

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Statement of Purpose: Polyurethane biostability has been the subject of intense research since the failure of polyether polyurethane pacemaker leads in the 1980s. Recently, temperature accelerated *in vitro* testing and time temperature superposition (TTS) have been used in an attempt to predict the *in vivo* biostability of polydimethylsiloxane (PDMS) based polyurethanes (SPU), specifically, that these materials may be susceptible to bulk hydrolysis *in vivo*.[1] A critical assumption in TTS is that all components of a polymer must respond equally to temperature in the temperature range being tested.[2] This assumption typically holds true for homogeneous polymers, but generally does not hold true for multi-phase systems, such as SPUs. In this study, differential scanning calorimetry (DSC), dynamic mechanical thermal analysis (DMTA), and water absorption studies were performed on Elast-Eon^{TM} 2A (E2A), a SPU, in order to test the validity of this crucial assumption and the application of TTS to this polymer.

Methods: E2A (AorTech International) was received from the manufacturer. E2A is a SPU with a Shore hardness of 90A. E2A consists of hard segments of 4,4'-methylenediphenyl diisocyanate (MDI) and 1,4-butanediol (BDO) and mixed soft segments of PDMS and poly(hexamethylene oxide) (PHMO) in a ratio of 80:20. E2A is used as insulation on cardiac leads under the name Optim^{TM} (St. Jude Medical). DSC was performed on compression molded E2A samples using a Perkin Elmer Pyris 6 DSC. Heating scans were made from -30 °C to 120 °C with a heating rate of 20 °C/min. DMTA was performed on E2A tubing samples using a TA Instruments RSA G2-strain controlled DMTS in tensile mode. A constant frequency of 1 Hz and constant strain of 0.1% were used while heating the samples from 35 °C to 85 °C using steps of 5 °C. Water absorption testing was performed on compression molded E2A samples. Water absorption testing was performed at 37 °C, 55 °C, 70 °C, and 85 °C and gravimetric analysis was used to measure the water absorption at several time points during the study.

Results: DSC of E2A revealed an endothermic transition with an onset near 45 °C and a maximum near 60 °C. DMTA of E2A demonstrated non-linear log-log plots of storage modulus (E'') versus loss modulus (E') with an inflection point at approximately 65 °C (Figure 1). Deviation in these plots from linearity indicate changes in the morphological state of the polymer.[2] Water absorption studies showed that the equilibrium water uptake by E2A increased consistently with temperature, absorbing 40% more moisture at 85 °C than at 37 °C (Figure 2). The saturation level, M_{sat}, followed an Arrhenius form: $M_{sat} = M_{(sat,0)} \exp(-\Delta H_s/RT)$ where $M_{(sat,0)}$ is a constant and ΔH_s is the enthalpy of mixing.[3] A plot of ln M_{sat} versus 1/T was linear and the slope was used to estimate an enthalpy of mixing of 6.3 kJ/mol for E2A. In the previous temperature accelerated *in vitro* study, the authors made an assumption of constant water concentration (uptake) with temperature when building their TTS model and attempting to predict the *in vivo* biostability of E2A.[1] The current water absorption results indicate that this assumption was invalid.

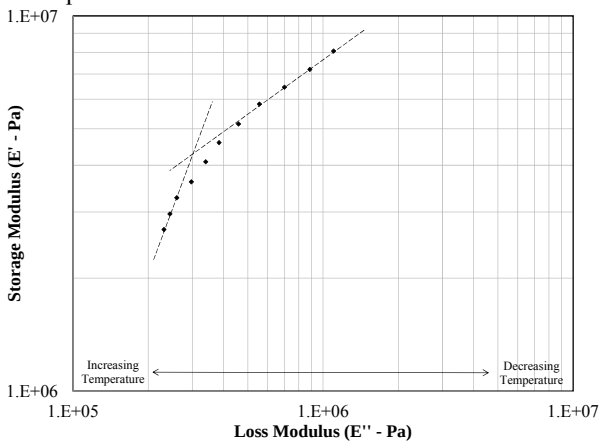

Figure 1. *DMTA storage modulus versus loss modulus for Elast Eon^{TM} 2A as temperature increased from 35 – 85 °C. Dashed lines indicate an inflection point and deviation from linearity.*

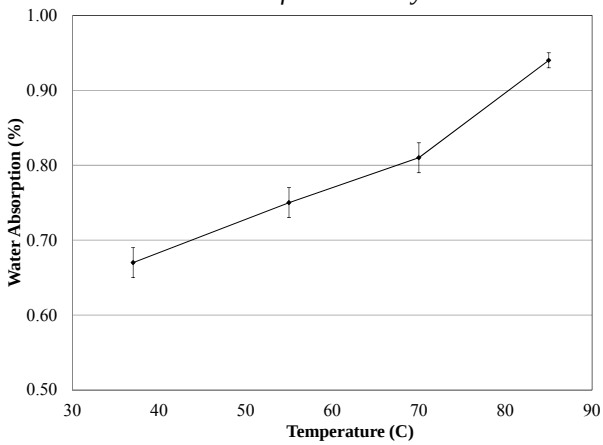

Figure 2. *Water absorption percentages at saturation versus temperature for Elast Eon^{TM} 2A.*

Conclusions: The DSC and DMTA results indicate that a phase transition or morphological change occurs in E2A near 60 °C. These results indicate that the key assumption required for the use of TTS is violated in E2A in this temperature range. Water absorption results showed that the equilibrium water uptake by E2A increased consistently with temperature. These results indicate that the assumption of constant water concentration (uptake) with temperature made in a previous study was invalid. Thus, the current results clearly highlight limitations in predicting the *in vivo* biostability of SPUs using TTS.

References:

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