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A biokinetic model for nickel released from cardiovascular devices

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Abstract

Many alloys used in cardiovascular device applications contain high levels of nickel, which if released in sufficient quantities, can lead to adverse health effects. While nickel release from these devices is typically characterized through the use of in–vitro immersion tests, it is unclear if the rate at which nickel is released from a device during in–vitro testing is representative of the release rate following implantation in the body. To address this uncertainty, we have developed a novel biokinetic model that combines a traditional toxicokinetic compartment model with a physics–based model to estimate nickel release from an implanted device. This model links the rate of in–vitro nickel release from a cardiovascular device to serum nickel concentrations, an easily measured endpoint, to estimate the rate and extent of in–vivo nickel release from an implanted device. The model was initially parameterized using data in the literature on in–vitro nickel release from a nickel–containing alloy (nitinol) and baseline serum nickel levels in humans. The results of this first step were then used to validate specific components of the model. The remaining unknown quantities were fit using serum values reported in patients following implantation with nitinol atrial occluder devices. The model is not only consistent with levels of nickel in serum and urine of patients following treatment with the atrial occluders, but also the optimized parameters in the model were all physiologically plausible. The congruity of the model with available data suggests that it can provide a framework to interpret nickel biomonitoring data and use data from in–vitro nickel

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