Fitting of a prosthetic socket is a critical stage in the process of rehabilitation of a trans-tibial amputee (TTA). To date, prosthetic fitting typically depends on the subjective skills of the prosthetist, and is not supported by biomedical instrumentation that allows evaluation of the quality of fitting. Specifically, no technology is presently available to provide real-time continuous information on the internal distribution of mechanical stresses in the residual limb during fitting of the prosthesis, or while using it, and this severely limits patient evaluations. In this study, a simplified yet clinically-oriented patient-specific finite element (FE) model of the residual limb was developed for real-time stress analysis. For this purpose we employed a custom-made FE code that continuously calculates internal stresses in the residual limb, based on boundary conditions acquired in real-time from force sensors, located at the limb-prosthesis interface. Validation of the modeling system was accomplished by means of a synthetic phantom of the residual limb. Human studies were conducted subsequently in 5 TTA patients. The dimensions of bones and soft tissues were obtained from x-rays of the residual limb of each patient. 7 force sensors were placed at the stump/liner interface, and subjects walked on a treadmill during analysis. Generally, stresses under the shinbones were ~3-fold higher than stresses at the soft tissues behind the bones. Usage of a thigh corset decreased the stresses in the residual limb during gait by ~80%. Also, the stresses calculated during the trial of a subject who complained about pain were the highest, suggesting a problematic stump or prosthesis. We conclude that real-time patient-specific FE analysis of internal stresses in deep soft tissues of the residual limb in TTA patients is feasible. This method is promising for improving the fitting of prostheses in the clinical setting and for protecting the residual limb from muscle flap necrosis and deep pressure ulcers.