Abstract

**Background and Significance:**
Vertebral fractures are the most common complication of osteoporosis, often leading to pain, height loss, disfigurement, respiratory impairment, depression, and decreased life span. Approximately 30-50% of individuals over age 50 have at least one vertebral fracture, and the presence of an initial fracture is among the strongest risk factors for a subsequent vertebral fracture. Indeed, 20% of women with a vertebral fracture suffer another vertebral fracture within a year, a phenomenon known as the "vertebral fracture cascade." However, the reasons underlying this marked increase in fracture risk following a first vertebral fracture are largely unknown. A possible mechanism, which is supported by preliminary studies from our laboratory, is that an initial vertebral deformity alters spinal loading, which then increases risk of future vertebral fracture. However, it is unclear what activities are most likely to result in a vertebral fracture since the majority of fractures occur without specific trauma, and patients are often unable to identify the causative event. Additionally, vertebral fractures occur most often in the mid-thoracic and thoracolumbar regions of the spine, and it is not clear if different mechanisms are responsible for mid-thoracic versus thoracolumbar fractures. The main objectives of this project are: 1) to determine the contribution of altered spinal loading to vertebral fracture risk and 2) to identify the activities and biomechanical mechanisms responsible for mid-thoracic and thoracolumbar vertebral fractures. Prior efforts to understand the contribution of altered spine mechanics to vertebral fractures have been limited by the inability to accurately assess in vivo spinal loading, especially in the thoracic spine.

**Specific Aims:**
To achieve the aforementioned objectives, we propose three specific aims: 1) Develop an improved musculoskeletal spine model to facilitate patient-specific estimates of vertebral loading in the thoracic and lumbar spine; 2) Determine the effects of vertebral fracture on spinal loading; and 3) Identify which activities are most strongly associated with incident vertebral fracture.

**Methods:**
For Aim 1, an anatomically detailed musculoskeletal spine model will be developed using OpenSim software. The model will allow for patient-specific estimates of in vivo spine loading during various functional activities by incorporating individualized measurements of body size, spinal curvature, and muscle morphology measured from CT. In Aim 2, we will use individuals from the Framingham Heart Study who have both baseline and ~6-year follow-up CT scans to determine how vertebral fractures change spine loading and thus risk of future fracture. We will use our spine model, in combination with spinal curvature and muscle morphology measurements made from baseline and follow-up CT, to compute patient-specific estimates of vertebral loading before and after a fracture, and then compare this to the change in loading that occurs in control subjects who did not have a fracture during the follow-up period. In Aim 3 we will use our spine model to parametrically explore how body position and various functional activities affect spine loading. We will then use the model to determine what activities are most strongly associated with incident mid-thoracic and thoracolumbar vertebral fractures in the Framingham cohort.