Vitamin D deficiency or insufficiency is more common in primary hyperparathyroidism (PHPT) than in the general population. Clinical manifestations of PHPT are more severe in vitamin D deficient patients, and even in those with mild disease, patients with low vitamin D levels have higher PTH concentrations and bone turnover markers. Given the frequency of vitamin D deficiency in the PHPT population, it is likely that our current understanding of the biochemical and skeletal features of PHPT reflects an admixture of these two conditions. The central hypotheses of this proposal are that in patients with PHPT: 1) Vitamin D deficiency worsens the hyperparathyroid state and is associated with its own specific skeletal features; and 2) Repletion of vitamin D will ameliorate those aspects of the disease that are due to vitamin D deficiency, and thus reveal the true biochemical and skeletal phenotype of the underlying
disease. To test these hypotheses, this proposal will utilize state-of-the-art biochemical and skeletal imaging methods. The proposal has the following aims: 1. To compare PHPT patients with and without vitamin D deficiency in order to: a) determine the skeletal features of the hyperparathyroid state that are attributable to vitamin D deficiency; and b) to describe the skeleton in PHPT without the confounding effects of coexisting vitamin D deficiency. 2. To investigate the early effects of high dose vitamin D repletion on histomorphometric parameters of bone remodeling (by quadruple labeled bone biopsy). 3. To investigate the effects of three vitamin D repletion regimens on biochemical, denstometric, microarchitectural and biomechanical features of PHPT. This proposal will fulfill a key mandate of the Third International Workshop on Asymptomatic Primary Hyperparathyroidism (2008) to obtain more data on vitamin D deficiency in individuals with PHPT. The recently published International Consensus Guidelines on Asymptomatic PHPT (J Clin Endocrinol Metab 94:335-9, 2009) specifically call for measurement of 25-hydroxyvitamin D in all patients with PHPT, and repletion of low levels (<20 ng/ml). However, no recommendations for repletion were included in the Guidelines, because of limited data upon which to base them. This information is urgently needed, as are data on the effects of vitamin D treatment in PHPT upon clinically relevant endpoints such as bone density, skeletal microarchitecture, bone remodeling and bone strength. This proposal will therefore enhance our understanding of the skeleton in PHPT, while providing information that may help in formulating recommendations for vitamin D repletion, a key research goal of the new Consensus Guidelines, and an imperative for clinicians treating this disorder. The ultimate benefit will be to patients with PHPT, for whom clinical decision-making will be strengthened by data that have heretofore not been available.