Lay Summary

Project Title: Diagnosis of Renal Osteodystrophy in a Week: Kawamoto Cryosections as Rapid Alternative to Methyl Methacrylate Embedding and as a Platform for Molecular Bone Analyses

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Bone fragility is a major cause of fractures, pain, and disability. In patients with chronic kidney disease (CKD), bone becomes particularly fragile due to a condition known as **chronic kidney disease-mineral and bone disorder (CKD-MBD)**. These patients have a fracture risk that is up to five times higher than that of the general population. Different forms of CKD-related bone disease require different treatments, but they can only be reliably diagnosed by examining a bone biopsy under the microscope. Blood tests and imaging techniques cannot currently provide the same level of information.

The current gold standard for bone biopsy analysis is **bone histomorphometry**, which requires embedding bone tissue in a hard plastic (methyl methacrylate, MMA) before microscopic examination. While this method provides excellent structural information, it has important limitations. It is technically demanding, available only in a few specialized centers, and prevents the use of modern molecular techniques such as RNA sequencing that could reveal why bone disease develops and identify new treatment targets.

This project aims to validate an innovative alternative known as the **Kawamoto cryosection technique**. Instead of embedding bone in plastic, this method prepares thin frozen sections of mineralized bone while preserving both tissue structure and biological molecules. If successful, an individual bone sample could be used for both traditional histological evaluation and advanced molecular analyses.

To determine whether the new method is as accurate as the current gold standard, we will compare the two techniques using four complementary types of bone samples: bovine tail vertebrae, human bone obtained during biopsies or fracture surgery, and bone from mice labeled with tetracycline to assess dynamic bone formation. For each specimen, the same bone will be processed using both methods, and quantitative measurements of bone structure and remodeling will be directly compared.

Successful validation would establish a new methodological platform for bone research. By combining high-quality bone histology with molecular analyses, the Kawamoto technique could improve our understanding of diseases such as CKD-MBD and other metabolic bone disorders, assist in the discovery of new biomarkers and therapeutic targets, and maximize the scientific value obtained from the limited number of human bone biopsies available for research. The project has the change to directly change patient care by reducing the processing time of bone biopsies from over several weeks to a single week, and it can provide an essential foundation for future studies aimed at developing more precise diagnostic tools and personalized treatments for patients with bone disease.