ANALYTICAL IMPACT OF METHOD-DEPENDENT VARIABILITY IN BONE ALKALINE PHOSPHATASE IMMUNOASSAYS

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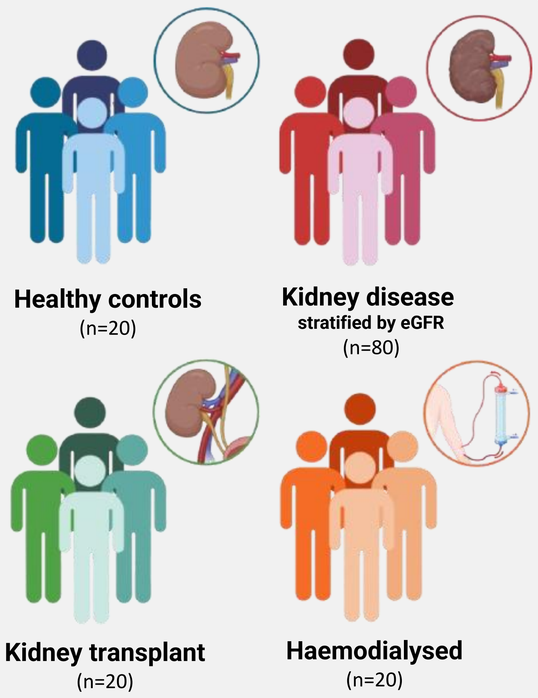
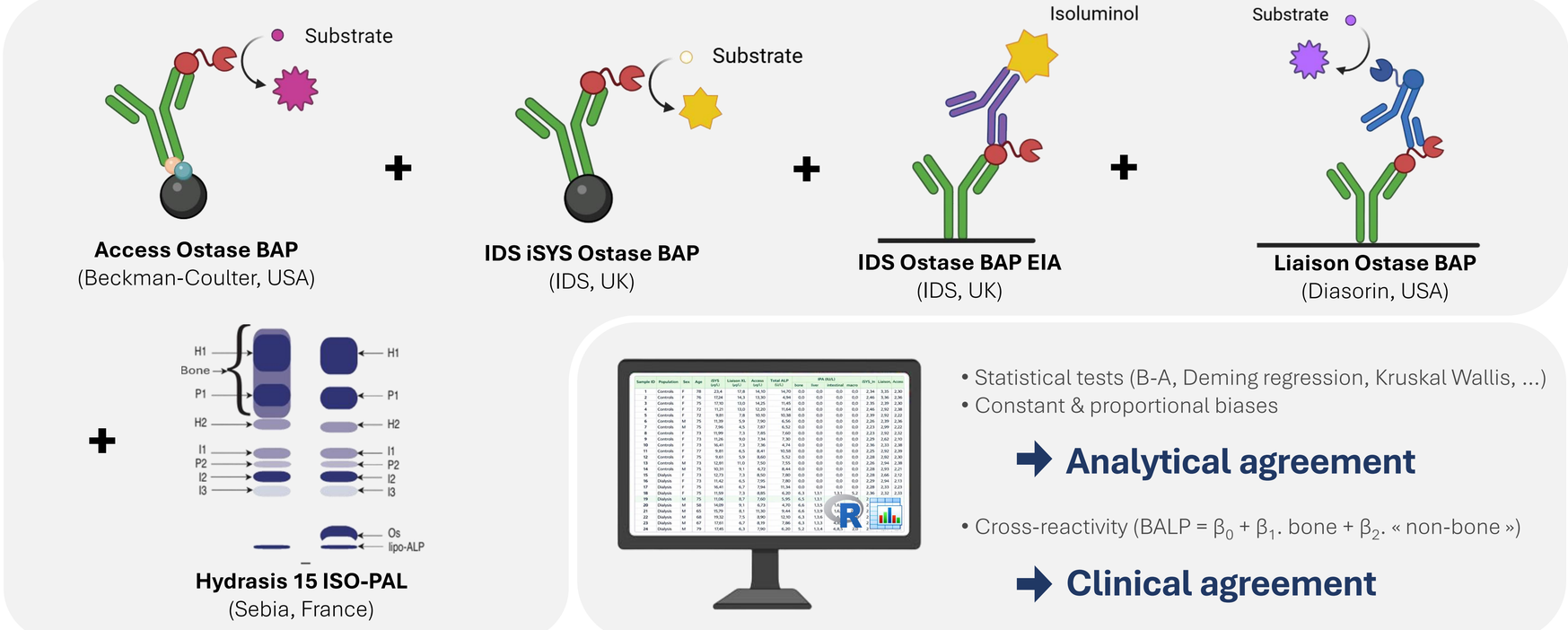
Introduction

Bone-specific alkaline phosphatase (BALP) is the biomarker recommended by the **KDIGO guidelines** for the assessment of bone turnover in CKD-MBD and has recently been proposed by the **ESCEO/IOF/IFCC consensus** as a **reference marker** of bone formation in CKD-associated osteoporosis. BALP measurement is routinely performed worldwide. However, the availability of multiple commercial BALP immunoassays may lead to discrepancies in patient results. This study compared the analytical performance and clinical agreement of four BALP immunoassays across distinct patient subgroups.

Materials and Methods





- Statistical tests (B-A, Deming regression, Kruskal Wallis, ...)
- Constant & proportional biases

➡ **Analytical agreement**

- Cross-reactivity (BALP = $\beta_0 + \beta_1$. bone + β_2. « non-bone »)

➡ **Clinical agreement**

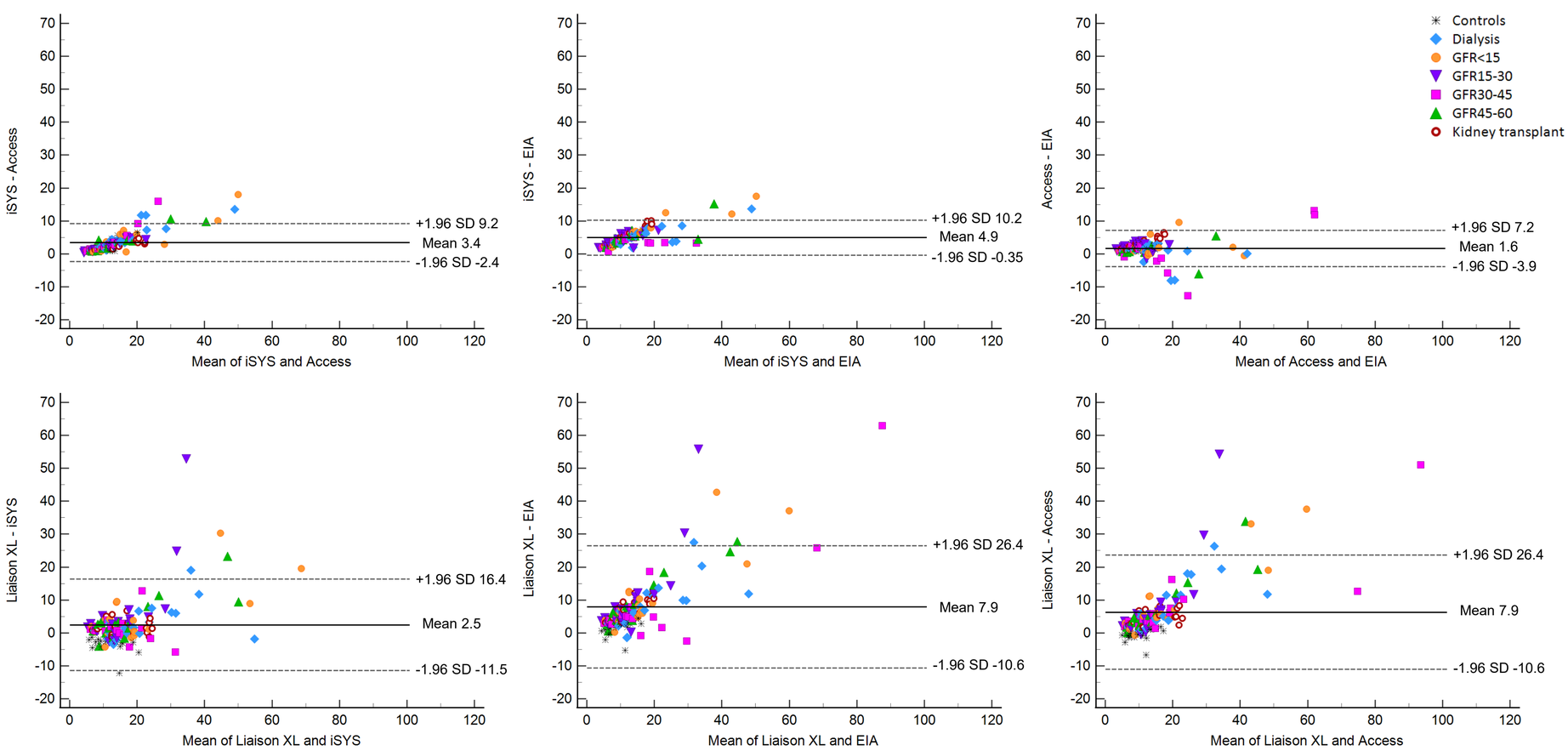
Results

Significant correlation was found for all assays pairs (Spearman's ρ = 0.816–0.984).

Bland-Alman analyses revealed systematic differences between methods, with largest biases in comparison involving the Liaison XL assay.

Some method pairs showed significantly higher biases in CKD, dialysis or kidney transplant patients compared with controls. (Kruskal-Wallis)

The estimated cross-reactivity (β_2/β_1) increased proportionally with the non-bone ALP fraction, indicating assay susceptibility to non-bone ALP isoenzymes.



Conclusion

Although correlation between methods are statistically significant, the observed biases indicate that the **assays are not interchangeable**. The larger biases observed in CKD, dialysis and kidney-transplanted patients further underscore the need for careful clinical interpretation. These findings reinforce the **importance of assay harmonization** and the **need for standardization**.

Perspectives

The development of a sensitive and highly specific method is crucial to overcome current assay limitations. **High-performance liquid chromatography coupled with mass spectrometry** represents a promising approach for the precise and reproductible quantification of BALP and BALP isoforms, ensuring improved diagnostic reliability and facilitating **standardization** efforts.