

## Background:

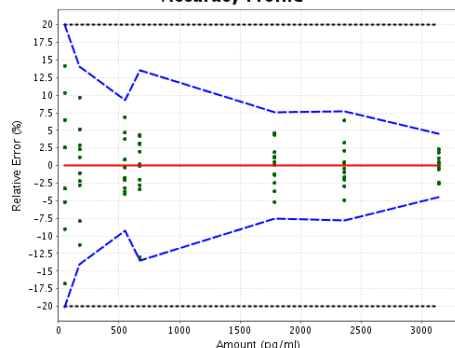
As of late 2010, IOF and IFCC recommended s-PINP and s-CTX as reference analytes for bone turnover markers in observational and intervention studies. We assessed the analytical performance of the IDS-iSYS Crosslaps (CTX-I) automated assay and compared this method to the Elecsys assay. The observed ranges for apparently healthy children and reference intervals for pre-menopausal, post-menopausal women and men were established.

## Materials and methods:

The accuracy profile was determined with 7 serum pool levels (0.05 – 3.12 ng/mL). The method linearity was verified with two sets of high/low serum samples. A total of 100 remnant serum samples [0.06-4.5ng/mL] was assayed by each method for method comparison. Serum specimens from overnight fasting, apparently healthy Caucasians subjects, normal Calcium, Phosphates, Intact PTH, and eGFR > 60, were selected to establish the reference intervals for males, pre-menopausal and post-menopausal (N = 120). The observed ranges were established with apparent healthy young (ages: 0.3 - 20 years) males (N = 287) and females (N = 295).

## Results

### Accuracy Profile



### Linearity

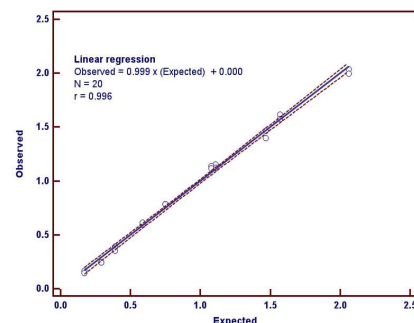


Fig. 2: IDS-iSYS CTX-I Linearity.

### Method comparison

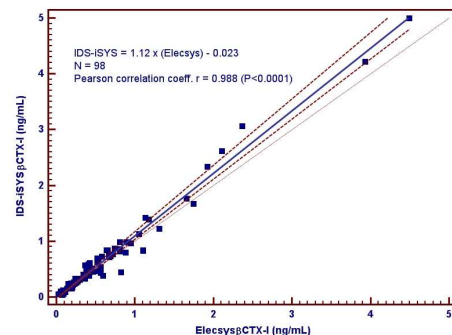


Fig. 3: Passing-Bablok regression IDS-iSYS vs. Elecsys βCTX-I.

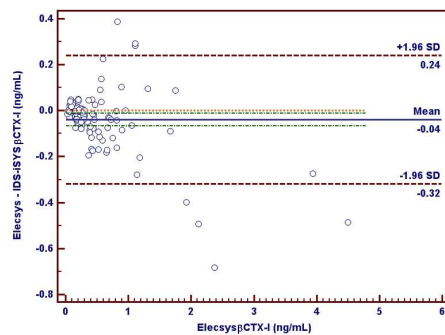


Fig. 4: Bland-Altman plot DS-iSYS vs. Elecsys βCTX-I.

## Reference intervals

The 95% double-sided reference interval for pre-menopausal, post-menopausal, and males was calculated (Table 1). The 5<sup>th</sup> – 95<sup>th</sup> percentile observed ranges for males (Table 2) and females (Table 3) <20 years of ages were stratified by every 2 years. The βCTX-I concentration changes with age and menopause. In boys, the levels tend to increase between the ages of 6-8 years and remains high until the age of 16. In girls, the βCTX-I also elevates between the 6-8 years old, but the levels decrease earlier than boys, between the ages of 12-14 (Fig. 5).

Populations	No. of Subjects	Age (year) (Mean±SD)	Median (ng/mL)	SD (ng/mL)	Mean (ng/mL)	95% CI. (ng/mL)
Pre-Menopausal	120	36.8 ± 8.0	0.20	0.17	0.23	0.03 - 0.66
Post-Menopausal	120	67.4 ± 6.7	0.29	0.23	0.34	0.04 - 0.92
Males	120	57.4 ± 16.4	0.3	0.19	0.31	0.02 - 0.80

Table 1: IDS-iSYS βCTX-I reference interval for adults.

Age Group	No. of Subjects	Median (ng/mL)	SD (ng/mL)	Mean (ng/mL)	5 <sup>th</sup> - 95 <sup>th</sup> (ng/mL)
0 - <2	30	740	161	748	472 - 1039
2 - <4	31	604	157	575	271 - 765
4 - <6	33	492	128	461	248 - 660
6 - <8	30	594	108	610	314 - 897
8 - <10	33	624	155	642	410 - 882
10 - <12	25	618	243	643	328 - 1169
12 - <14	24	772	301	764	194 - 1146
14 - <16	24	303	260	421	145 - 1015
16 - <18	25	144	125	196	66.7 - 436
18 - <20	26	92.4	83.6	110	27.2 - 34.3

Table 2: IDS-iSYS βCTX-I percentile ranges for males <20 years.

Age Group	No. of Subjects	Median (ng/mL)	SD (ng/mL)	Mean (ng/mL)	5 <sup>th</sup> - 95 <sup>th</sup> (ng/mL)
0 - <2	23	879	256	817	364 - 1188
2 - <4	28	556	186	512	194 - 757
4 - <6	35	580	178	587	304 - 966
6 - <8	31	596	159	616	390 - 937
8 - <10	31	712	237	727	394 - 1108
10 - <12	25	644	223	700	388 - 1094
12 - <14	29	272	184	332	82.0 - 650
14 - <16	29	102	77.4	130	53.8 - 300
16 - <18	33	70.0	31.9	75.0	25.1 - 148
18 - <20	31	48.2	28.1	54.7	24.1 - 118

Table 3: IDS-iSYS βCTX-I percentile ranges for females <20 years

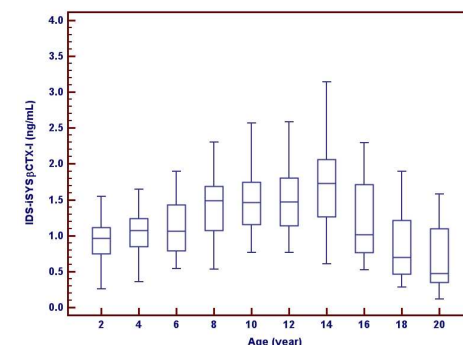


Fig. 5: IDS-iSYS βCTX-I age related distribution for males <20 years

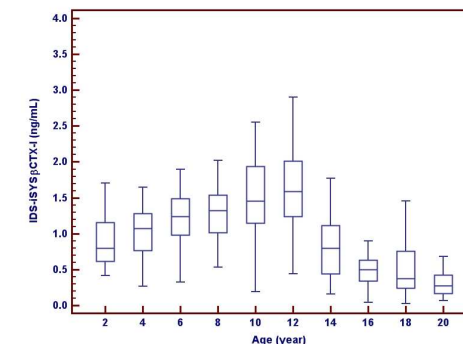


Fig. 6: IDS-iSYS βCTX-I age related distribution for females <20 years

## Conclusions:

- The IDS-iSYS CTX-I demonstrated suitable characteristics as a high throughput, fully automated bone resorption assay for clinical laboratories.
- The established pre-menopausal, post-menopausal, and males reference intervals will be useful tool for the monitoring of osteoporosis therapeutic treatment.
- Values from more than 500 children classified according to age and gender would be helpful to clinical laboratories and pediatricians.