HEALTH SERVICES LABORATORIES

Chromogranin A – Patient and sample comparison DiaSource vs Kryptor

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Introduction

Chromogranin A (CgA) is a tumour marker used for the diagnosis, monitoring and prognosis of neuroendocrine tumours (NETs)[1]. To address the increasing demand on the laboratory a new, higher throughput and fully automated platform was assessed; the Kryptor Compact Plus CgA II. The Kryptor was compared against the laboratories' current DiaSource CgA method. In adjunct, we determined whether samples needed to be taken on ice into aprotinine EDTA (trasylol) tubes or plain EDTA tubes collected at room temperature, with plasma separated within 48 hours.

Methods

A total of 60 concurrent trasylol and plain EDTA samples were compared to one another using paired t-tests and linear regression analysis. Samples that encountered analytical errors were omitted from analysis. Data analysis and visualisation was performed using R studio version 2024.09.0+375. Ethics was not required for this laboratory improvement study, as spent samples

Results

A significant difference was observed between the assays. The DiaSource produced higher results compared to the Kryptor for both tube types. Trasylol (n = 58, p = 0.031, y = 0.459x + 3.35, R^2 = 0.87) and EDTA (n = 57, p = 0.027, y = 0.451x +2.71, R^2 = 0.90).

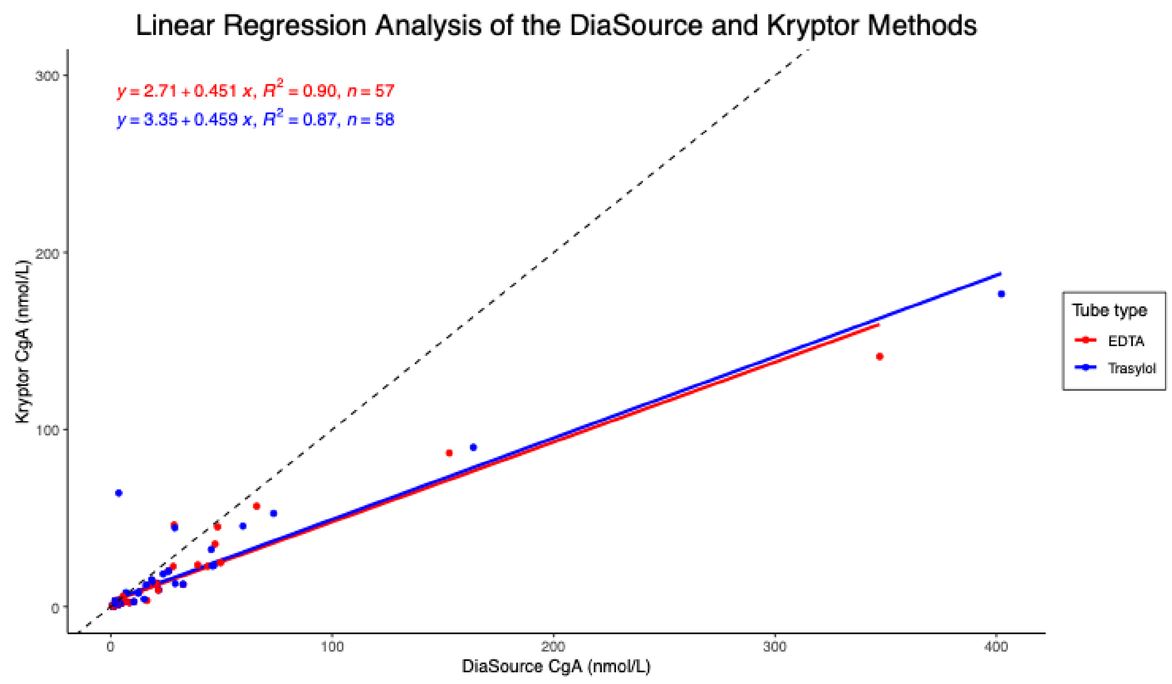

Figure 1. Linear regression of the DiaSource and Kryptor methods using trasylol and EDTA tubes.

However, tube type did not appear to have an effect on CgA results using either the DiaSource (n = 58, p = 0.725, y = 1.14x – 1.79, R^2 = 0.99) or Kryptor platform (n = 56, p = 0.737, y = 1.14x – 1.40, R^2 = 0.98).

Discussion

Our findings highlight that although there is no significant difference between the two sample types there is a significant difference between the two assays (figure-1). This difference was mirrored almost identically between the trasylol and EDTA tubes; with the Kryptor reporting CgA results approximately 50% lower than the DiaSource assay (figure-2).

The observed difference is likely due to the formulation of the assays as the antibodies used in both assays target different CgA epitopes. The DiaSource uses a sandwich principle enzyme linked immunoassay, with antibodies liberated against CgA residues 236-251 and 264-279, whereas the Kryptor's time resolved cryptate emission (TRACE™) method uses antibodies directed to residues 124-144 and 280-301[2]. This does raise the issue regarding assay standardisation. As yet there is no CgA reference standard for manufacturers to formulate their assays to.

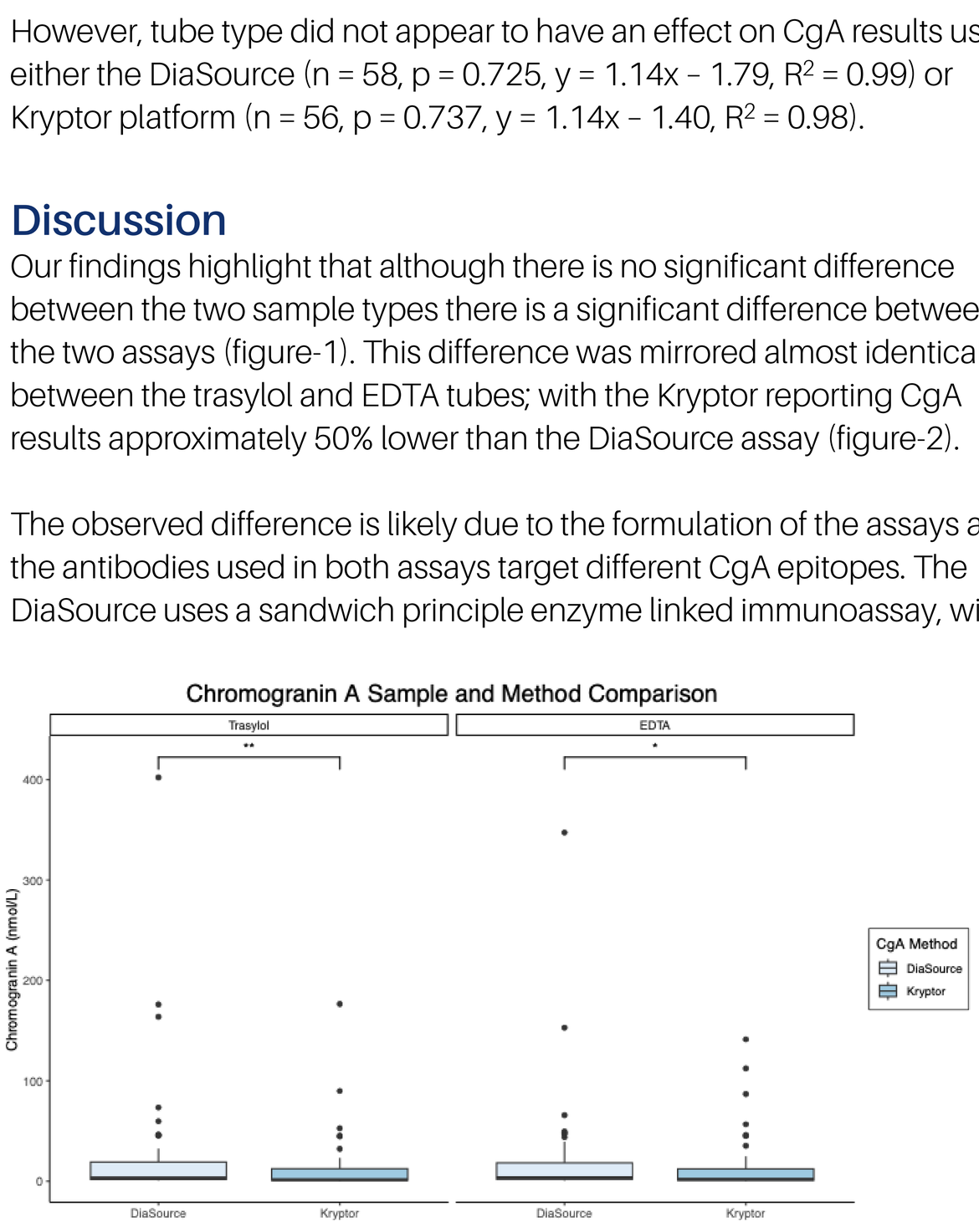

Figure 1. Boxplot of DiaSource and Kryptor methods grouped by sample type.
** p = 0.031, * p = 0.027

Although a significant difference was observed between the two methods each have different clinical cut offs. The DiaSource method has a cut off of 2.3 nmol/L whereas the Kryptor's cut off of 1.6. When applied to the respective data sets 8 more trasylol samples using the Kryptor method were below the cut off compared to the DiaSource. A similar picture was observed with the EDTA samples, where 7 EDTA samples were below the cut off.

Conclusion

This study is the first to assess the performance of the Kryptor CgA II assay to the DiaSource ELISA and to illustrate the significant difference between the two. The difference observed has the potential to impact patient care if transitioning from one method to the other; especially for monitoring purposes. As a result, it would be prudent to baseline patients with known NETs using both assays when transitioning between the two.

The data also demonstrates that samples do not not have to be collected on ice and into trasylol tubes. Thereby streamlining the collection process and potentially lowering sample rejection rates whilst reducing consumable costs.

Finally, this study has highlighted the need for further work evaluate CgA results in light of disease burden to elucidate which method has greater sensitivity and specificity in our patient cohort.

References

1. Ramage, J. K. et al. Guidelines for the management of gastroenteropancreatic neuroendocrine (including carcinoid) tumours (NETs). Gut 61, 6–32 (2012).
2. Krabbe, J. G., Monaghan, P. J., Russell, J., & de Rijke, Y. B. (2016). Analytical evaluation of a second generation assay for chromogranin A; a dual-site study. Clinical Chemistry and Laboratory Medicine, 54(4), e139-42.