

User guide for Kappa/ Lambda dot plot: Excel 2003 and 2007

This plot is to be used as a guide only. A clinical diagnosis should be made using a combination of serum free light chain (FLC) results in combination with other laboratory tests and clinical findings.

The Freelite Dot Plot Add-in

Add-ins are programs that add optional commands and features to Microsoft Excel. Before you can use an add-in, you must install it on your computer and then load it in Microsoft Excel. Add-ins (*.xla files) are installed by default in the Library folder in the Microsoft Excel folder. However, you may save the add-in anywhere that is accessible to your PC. Loading an add-in makes the feature available in Microsoft Excel and adds any associated commands to the appropriate menus. To conserve memory, unload add-ins you do not use often. Unloading an add-in removes its features and commands from Microsoft Excel, but the add-in program remains on your computer so you can easily load it again.

Installation

Download the Add-in from the Distributor Portal and save to an accessible location on your computer.

In Excel 2003: In an open workbook go to the Tools menu and click on the 'Add-Ins...' menu. Browse to the location where you saved the .xla Add-in file, select the .xla file and click ok. If you are asked to save the file to the Add ins folder say yes.

In Excel 2007: In an open workbook click on the Microsoft Office round button. Click Excel options and then click on Add-Ins. From the drop down 'Manage' menu select Excel Add-Ins and press go. Browse to the location where you saved the .xla Add-in file, select the .xla file and click ok. If you are asked to save the file to the Add ins folder say yes.

Unload an add-in program from Microsoft Excel

Open Excel, select the Tools menu from the top toolbar and click Add-Ins. In the Add-Ins available box, clear the check box next to the add-in you want to unload.

Note: When you unload an add-in from Microsoft Excel, it is not removed from your computer system.

Using the Freelite Dot Plot Add-in

Having downloaded, installed and loaded the Dot Plot Add-in, you are ready to use Excel to plot Freelite results.

Open a new workbook.

To plot your data points, input your serum FLC data into any range of empty cells in an Excel workbook. For clarity input data as two separate columns, data must be numeric and individual cells must not contain zero or null values. **Use mg/ L units.** For example:

| Patient ID | Kappa serum FLC (mg/L) | Lambda serum FLC (mg/L) |
|------------|------------------------|-------------------------|
| 1 | 100 | 120 |
| 2 | 50 | 70 |
| 3 | 20 | 25 |

The Add-in will either be on the main menu toolbar (In Excel 2003) or on the Add-in tab of the Microsoft Office ribbon (in Excel 2007). Click on The Binding Site and then Kappa/Lambda data plot. This will open the data selector, where you can select your kappa values in the top box and lambda values in the lower box. Once data has been selected, click ok and the program will automatically generate a graph containing the data.

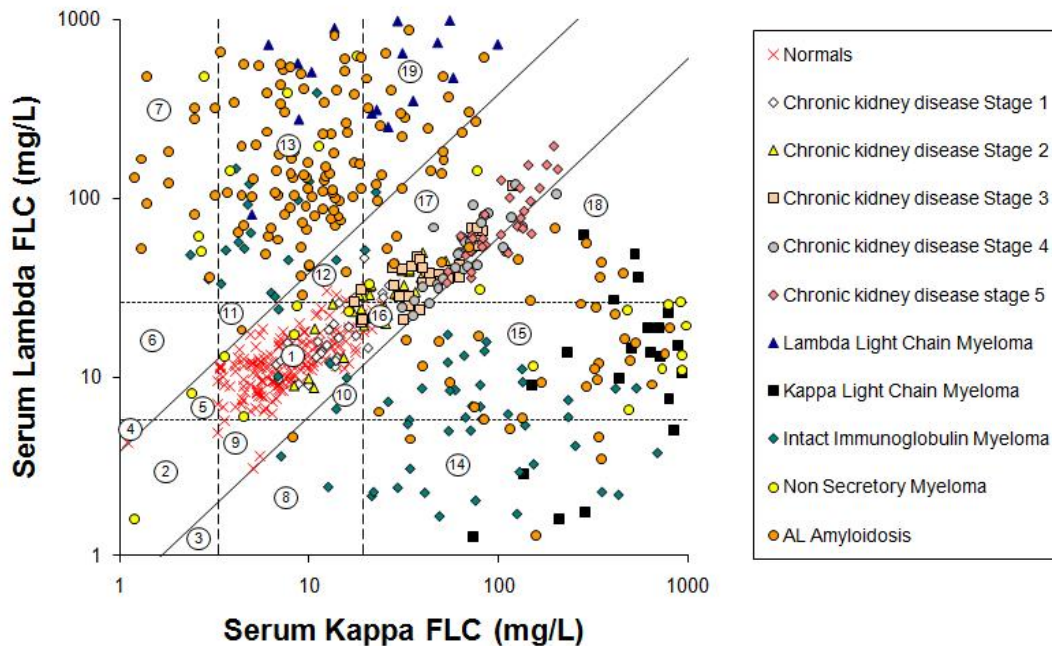


Figure 1. Serum kappa and lambda concentrations in a selection of clinical conditions. Patients are categorised according to serum free light chain concentrations and κ/λ ratios (see Table below). The axes are truncated for clarity.

Sample results can be considered under the following categories:

- a. Normal samples. The normal range for serum free light chains is described in chapter 5 of the book “Serum Free Light Chain Analysis (plus Hevylite),” 5th edition by AR Bradwell. If electrophoresis tests for monoclonal proteins are also normal it is most unlikely that the patient has a monoclonal gammopathy.
- b. Abnormal κ/λ ratios indicate a monoclonal gammopathy and should be investigated.
- c. Low concentrations of one or both light chains indicate a degree of bone marrow suppression, either from bone marrow replacement by the tumour or from tumour therapy.
- d. High concentrations of both light chains or the non-tumour light chain in patients with monoclonal gammopathies can be due to the following:-

- renal impairment
- over production of polyclonal light chains and probably intact immunoglobulins
- biclonal gammopathy of different light chain types.

Renal function tests and serum electrophoresis should be used to assess these different possibilities.

| | Kappa | Lambda | κ/λ | Interpretation |
|----|--------|--------|------------------|-----------------------------|
| 1 | Normal | Normal | Normal | Normal serum |
| 2 | Low | Low | Normal | BM suppression without MG |
| 3 | | | High | MG with BM suppression |
| 4 | | | Low | |
| 5 | | Normal | Normal | Normal serum/BM suppression |
| 6 | | | Low | MG with BM suppression |
| 7 | | | High | |
| 8 | | | Low | |
| 9 | Normal | | Normal | Normal serum/BM suppression |
| 10 | | Normal | High | MG with BM suppression |
| 11 | | | Low | |
| 12 | | High | Normal | plg or renal impairment |
| 13 | | | Low | MG without BM suppression |
| 14 | | High | Low | High |
| 15 | Normal | | | MG without BM suppression |
| 16 | | | Normal | plg or renal impairment |
| 17 | * | High | | |
| 18 | * | | High | MG with renal impairment |
| 19 | * | | Low | |

Table 1: Classification of monoclonal gammopathies according to serum kappa and lambda concentrations. BM = bone marrow; MG = monoclonal gammopathy; plg = polyclonal hypergammaglobulinemia.

* Included in the dot plot are a series of patients with increasing chronic kidney disease (CKD) stage. CKD is a progressive loss of renal function over a period of months or years and is identified by a blood test for creatinine. Higher levels of creatinine indicate a falling glomerular filtration rate (rate at which the kidneys filter blood) and as a result a decreased capability of the kidneys to excrete waste products. From the creatinine value, an estimated glomerular filtration rate can be calculated and this forms the basis of chronic kidney disease staging:

CKD stage 1: GFR >90 mL/min/1.73 m²

CKD stage 2: GFR 60-89 mL/min/1.73 m²

CKD stage 3: GFR 30-59 mL/min/1.73 m²

CKD stage 4: GFR 15-29 mL/min/1.73 m²

CKD stage 5: GFR <15 mL/min/1.73 m²

It has been demonstrated that borderline elevated κ/λ ratios can occur in patients with renal impairment but no other evidence of a monoclonal gammopathy. Borderline κ/λ ratios should be interpreted with circumspection. In patients with renal impairment, you may wish to use the published renal reference range; κ/λ ratio 0.37-3.1 (instead of 0.26-1.65) [1-3].

1. Hutchison, C.A., et al., *Quantitative assessment of serum and urinary polyclonal free light chains in patients with chronic kidney disease*. Clin J Am Soc Nephrol, 2008. **3**(6): p. 1684-90.
2. Hutchison, C.A., et al., *Serum free light chain measurement aids the diagnosis of myeloma in patients with severe renal failure*. BMC Nephrol, 2008. **9**(1): p. 11.
3. Abadie, J.M., K.H. van Hoven, and J.M. Wells, *Are renal reference intervals required when screening for plasma cell disorders with serum free light chains and serum protein electrophoresis?* Am J Clin Pathol, 2009. **131**(2): p. 166-71.