

See the patient road ahead more clearly with Hevylite[®] assays

Achieve greater clarity when monitoring IgA monoclonal proteins and overcome the laboratory challenges of electrophoresis.

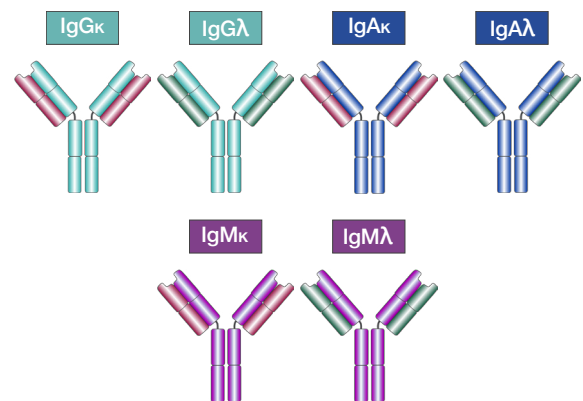
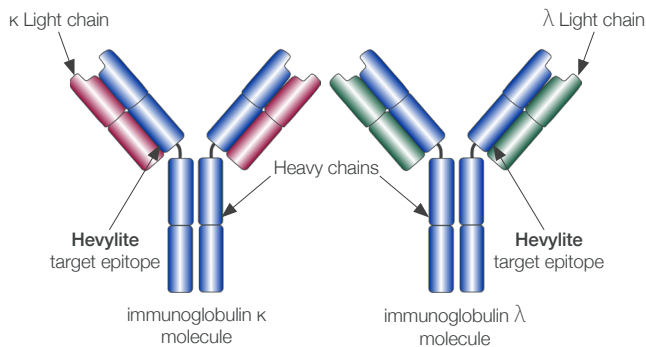


See the patient road ahead more clearly with Hevylite® assays

- ✔ Improved measurement of the involved heavy and light chain isotype.
- ✔ Hevylite assays provide unique information by measuring the uninvolved heavy and light chain (HLC) isotype which may provide a more complete clinical picture.
- ✔ Identify monoclonality even when total immunoglobulin measurement is normal.
- ✔ Achieve greater sensitivity when monitoring IgA monoclonal proteins.

What are Hevylite assays?

- ✔ Hevylite are six fully automated unique assays for the quantification of individual heavy + light chain isotypes in serum i.e. IgGκ, IgGλ, IgAκ, IgAλ, IgMκ and IgMλ. Only available on the Optilite® system.
- ✔ The IgGκ, IgGλ, IgAκ and IgAλ Hevylite assays can aid in the identification of plasma cell clonality through calculation of the heavy + light chain (HLC) ratio.
- ✔ They measure both the involved and uninvolved immunoglobulin.
- ✔ Hevylite assays uniquely measure the uninvolved heavy and light chain (HLC) – which may provide information not available with standard paraprotein assessments (SPE, CZE, sIFE, total immunoglobulins).



Hevylite assays provide additional valuable information through a range of unique and informative results.

Hevylite assays terminology

Term	Definition	For an IgAκ patient
HLC	Heavy + light chain isotype	
iHLC	Involved heavy + light chain isotype	IgAκ
uHLC	Uninvolved HLC	IgAλ
HLC ratio	E.G. IgAκ/IgAλ	IgAκ/IgAλ
dHLC	Involved HLC minus uninvolved HLC	IgAκ-IgAλ
HLC pair suppression	When the concentration of the uHLC is below the normal reference interval	Reduced concentration of IgAλ

Assay results should be used in conjunction with other laboratory tests and clinical evaluations.

To discuss the Hevylite assays in more detail, arrange to discuss with one of Binding Site's scientific experts.

Hevylite IgG and IgA Kappa and Lambda assays can identify monoclonality even when total immunoglobulin measurement is within normal range

- ✧ An abnormal IgA Hevylite ratio may identify monoclonality even when total IgA measurement is normal (see sample 2 in table 1).
- ✧ The HLC ratio may be more informative about the status of a patient's disease than the total immunoglobulin value.

International guidelines recognise the limitations of electrophoresis for IgA and suggest quantifying with total IgA assays¹. However, total IgA values do not distinguish between monoclonal IgA and the polyclonal background IgA. For example, if the total IgA measurement is normal e.g. 3 g/L – how much of that is polyclonal IgA or monoclonal IgA? (Table 1).

Table 1

	IgAk	IgAλ	Total IgA	IgAk/IgAλ	Hevylite Ratio
1.	1.8 g/L	1.2 g/L	3 g/L	1.5	Normal
2.	2.75 g/L	0.25 g/L	3 g/L	11	Abnormal

An abnormal IgA Hevylite ratio may be due to an increase in the involved heavy and light chain isotype, or the suppression of the uninvolved heavy and light chain isotype (Table 1).

Normal IgAk/IgAλ ratio in human serum: 0.911 - 2.416

Hevylite assays can help when electrophoresis is difficult to interpret

Electrophoresis is prone to a range of problems and paraproteins can co-migrate with other serum proteins making quantification difficult. Hevylite assays can overcome this problem as they specifically detect the HLC isotype present in the sample.

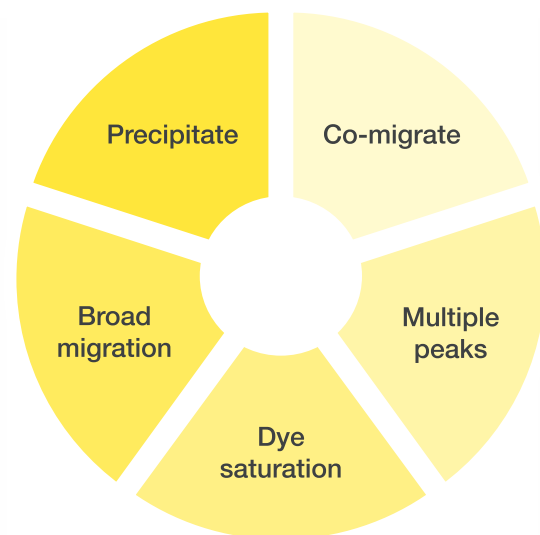


Table 2

IgA Multiple Myeloma	N	Accurate measurement not possible by SPE	Abnormal Hevylite Ratio	Total IgA abnormal
Boyle, 2014 ²	157	33%	100%	90%
Elssner-Freund, 2015 ³	88	31%	93%	
Ludwig, 2013 ⁴	56	46%	100%	
Amolak, 2013 ⁵	53	80%	100%	67%
Bengoufa, 2010 ⁶	50	46%	100%	
Steele, 2010 ⁷	31	74%	100%	
Total	435	44%	99%	

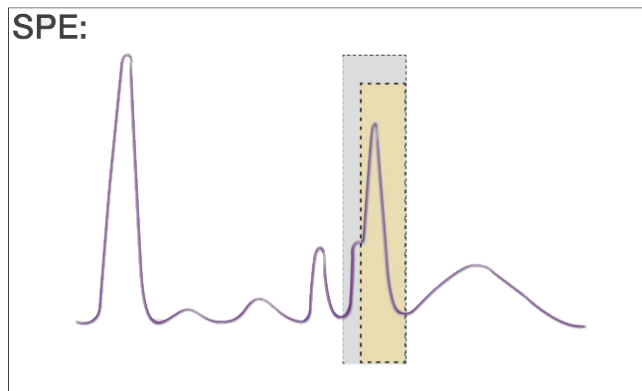
N = number of patients

In studies of more than 430 patients, 44% of IgA monoclonal proteins were not measurable by SPE but 99% had an abnormal Hevylite ratio indicating monoclonality (Table 2).²⁻⁷

Hevylite assays can overcome the challenge of co-migrating IgA monoclonal proteins

Measuring IgA monoclonal proteins that co-migrate in the β -region with SPE is sometimes difficult, making it challenging to monitor disease. Figure 1 shows a monoclonal protein peak co-migrating in the β_2 region in SPE densitometry, possibly leading to inaccurate results. In this particular patient, Hevylite identifies a raised IgAk concentration, an abnormal IgAk/IgA λ ratio, and suppression of the uninvolved IgA λ (see Table 3).

Figure 1



“HLC (Hevylite®) assays can be used to monitor IgA MM and provide similar information to the combination of SPEP, IFE, and total IgA quantification. Triaging of β -migrating IgA MM samples to IgA HLC assays should simplify monitoring of these patients.”⁸

Table 3 - Hevylite results

IgAk	IgA λ	IgAk/IgA λ
35.20	0.18	195.56

Red - abnormal, high

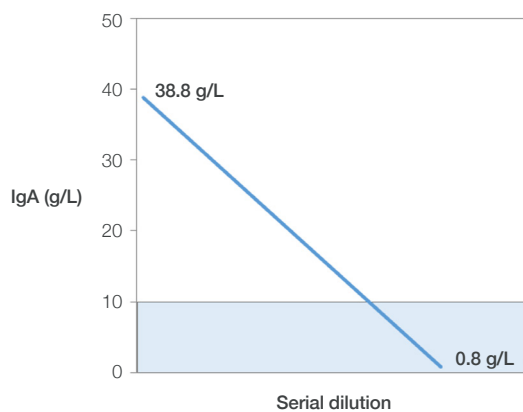
Blue - abnormal, suppressed

Hypothetical patient example demonstrating increase of the involved HLC, suppression of the uninvolved HLC and abnormal IgA κ/λ ratio (Table 3).

Table 4 - Normal ranges for IgA assays values in serum

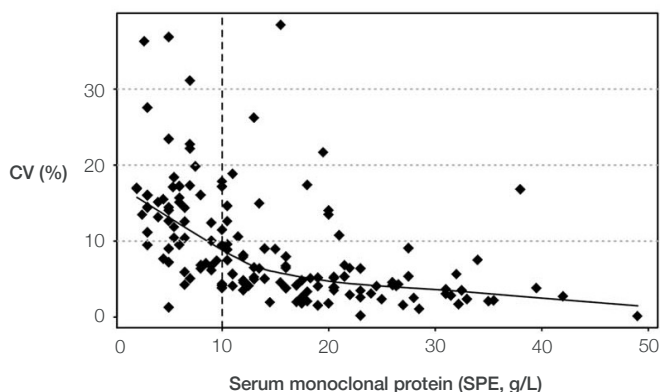
	95 Percentile range for Optilite analyser
IgA Kappa (g/L)	0.588 - 2.984
IgA Lambda (g/L)	0.432 - 2.035
IgA Kappa / IgA Lambda ratio	0.911 - 2.416

Figure 2 - Hevylite assays are more sensitive when measuring IgA than SPE and allow measurement of low levels of protein <10 g/L



Adapted from Eckold Clin Lab 2014;60:1491-500

Figure 3 - Monoclonal protein quantitation by electrophoresis is inaccurate <10 g/L



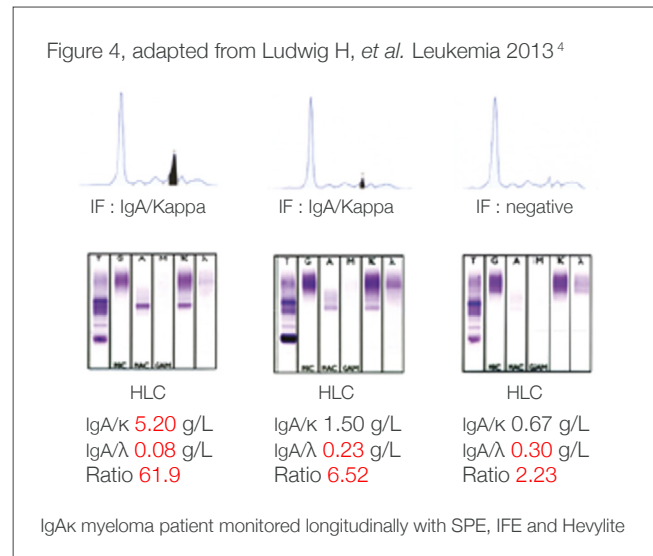
Katzmann Clin Chem 2011;57:1687-92

Hevylite assays are a sensitive tool to aid in the management of patients with multiple myeloma

In Figure 4 when immunofixation and SPE have normalised, Hevylite assay results show suppression of the uninvolved IgA, possibly indicating residual disease.

“The increased sensitivity of Hevylite assays can indicate the presence of residual disease in patients classified as being in Complete Response by other methods”⁴

“The HLC assays allow new ways to examine plasma cell biology and disease. We are able to identify abnormalities that were previously hidden from our view...”⁹



The challenge of measuring co-migrating monoclonal proteins was highlighted by Katzmann *et al.*⁸

In 2 studies where IgA Multiple Myeloma (MM) patients were monitored (Table 5), the Hevylite ratio detected monoclonality in considerably more patients than SPE.

Table 5 - Improved detection of monoclonality during monitoring

IgA Multiple Myeloma	N	Possible to measure by SPE	Abnormal Hevylite Ratio	IFE positive	Total IgA abnormal
Katzmann, 2015 ⁸	119	15%	45%	50% (IFE performed in 111 samples)	40%
Lakomy, 2013 ¹⁰	16	44%	75%	69%	
Total	135	19%	49%		

Hevylite assay results are abnormal in 49% of samples vs. 19% using SPE (Table 5).^{8,10}

Table 6 - Comparison of information

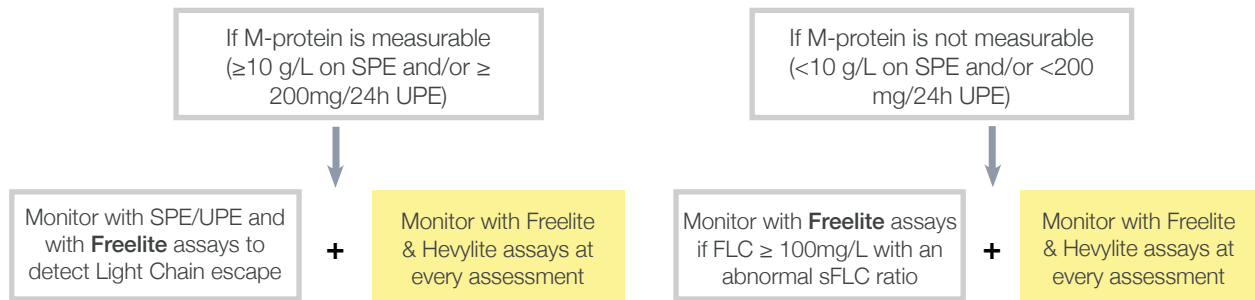
	Hevylite	SPE	IFE
Quantification of monoclonal protein	✓	✓	✗
Avoids subjective interpretation	✓	✗	✗
Accurate measurements below 10 g/L	✓	✗	✗
Quantification of uninvolved HLC (unique immunosuppression data)	✓	✗	✗


- ✓ Provides greater sensitivity than electrophoretic methods.
- ✓ Overcomes challenges such as co-migration, non-linearity and dye saturation.
- ✓ Optimises workflow through automation, reducing hands on time.
- ✓ Avoids subjective interpretation of gels by providing quantitative numerical results.
- ✓ May reduce the number of tests needed, especially for IgA monoclonal proteins.

Use Freelite® and Hevylite® assays for optimal management of multiple myeloma

Using both; Freelite assays and Hevylite IgG & IgA κ/λ assays, when monitoring multiple myeloma patients, identifies relapse of light chain and/or intact immunoglobulin clones.

Figure 5 - Freelite and Hevylite assays can optimise the management of multiple myeloma – A proposed algorithm. ^{13,14}



 Adapted from IMWG guidelines for diagnosis and monitoring of multiple myeloma ^{11,12}

Only IgG and IgA Hevylite assays are indicated for monitoring.

 Represent proposed additions

Ordering Hevylite assays

Kit	Product Code	Kit size	Measuring Range	Sample Type
Hevylite IgAk	NK623.OPT	50 test	0.018 - 112g/L	Serum, plasma
Hevylite IgAλ	NK624.OPT	50 test	0.016 - 104g/L	Serum, plasma
Hevylite IgMκ	NK625.OPT	50 test	0.02 - 150g/L	Serum, plasma
Hevylite IgMλ	NK626.OPT	50 test	0.018 - 135g/L	Serum, plasma
Hevylite IgGκ	NK621.OPT	50 test	0.115 - 120g/L	Serum, plasma
Hevylite IgGλ	NK622.OPT	50 test	0.075 - 105g/L	Serum, plasma

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Speak to your local Binding Site representative about how Hevylite assays can be implemented in your laboratory.

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