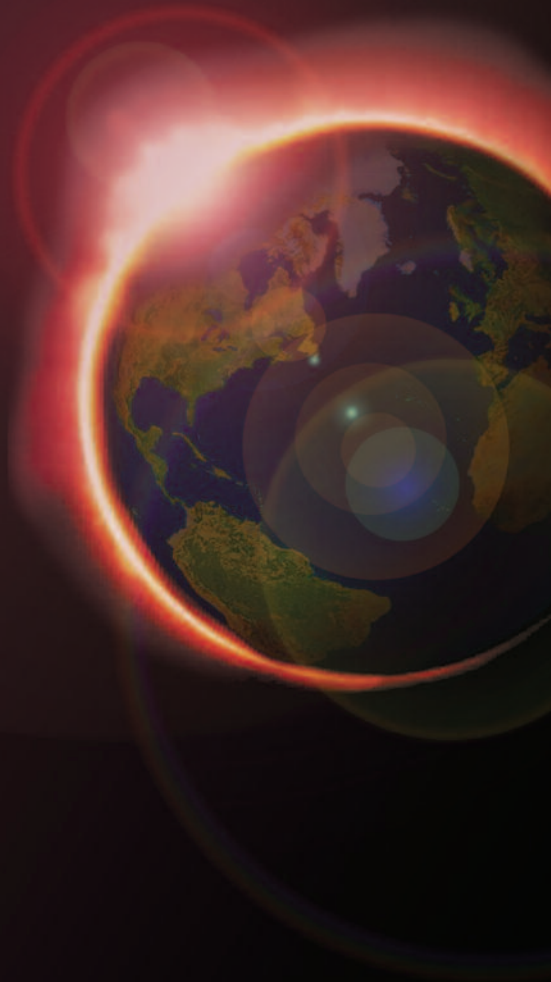


Monoclonal Gammopathy:
**A simple guide to Diagnosis
and Monitoring with Freelite™
serum free light chain assays**



Freelite™ serum free light chain assays

Freelite is a sensitive, specific marker of kappa and lambda free light chains (FLC) in serum and provides quantitative measurement of:

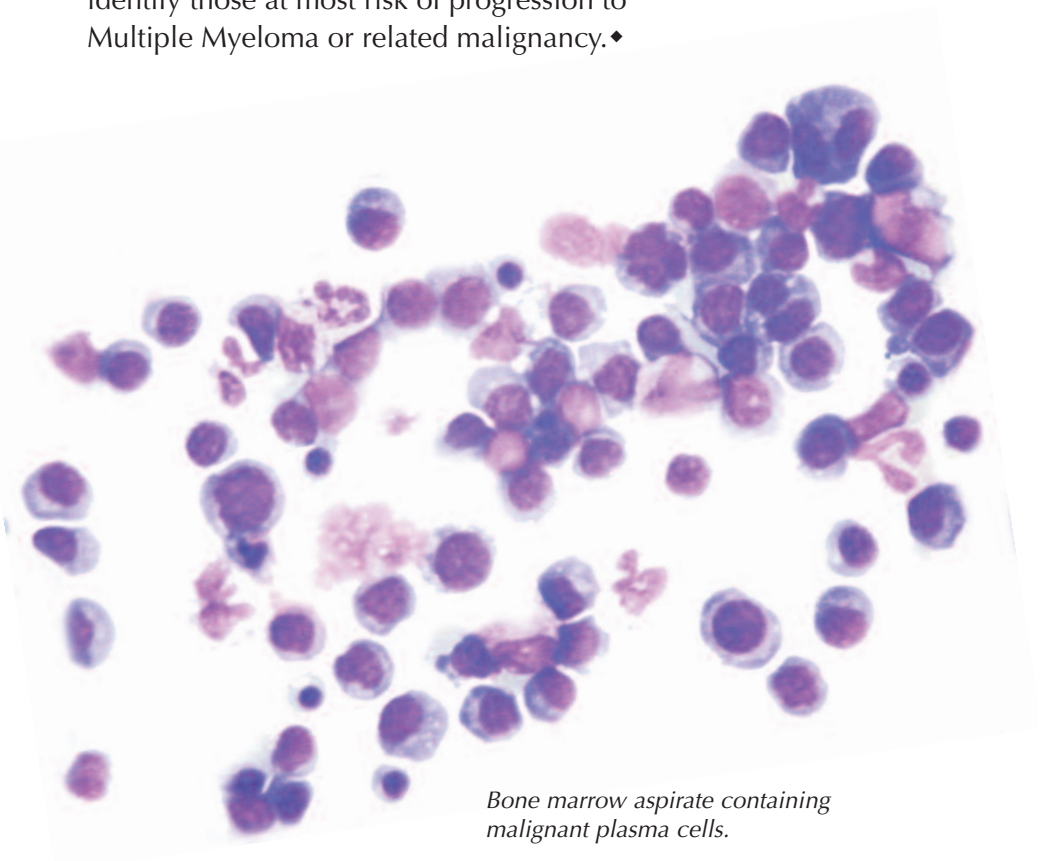
- free kappa in serum
- free lambda in serum
- the free kappa/free lambda ratio

The serum free light chain ratio is a strong indicator of monoclonality^{1,2,3} and is valuable for distinguishing monoclonal from polyclonal diseases.



Freelite can be used:

- to aid the diagnosis of B cell dyscrasia
- as an alternative to urinary Bence Jones Protein analysis^{3,4,5} when screening for monoclonal gammopathies
- to monitor the majority of Multiple Myeloma (MM) patients
- as a prognostic indicator to identify high risk patients
- to enable risk stratification of MGUS patients and identify those at most risk of progression to Multiple Myeloma or related malignancy.♦



Bone marrow aspirate containing malignant plasma cells.

♦The **Freelite** assay is not FDA cleared for use in risk stratification of MGUS patients in the USA.

Improve your detection of B cell dyscrasia

The inclusion of **Freelite** into laboratory protocols for diagnosis of monoclonal gammopathy will increase detection rates of B cell dyscrasia¹ without the added complications and difficulties of urine collection and testing.

Use **Freelite** with Serum Protein Electrophoresis or Capillary Zone Electrophoresis as part of the initial investigation and the high sensitivity of **Freelite** can identify patients missed by electrophoretic assays alone.^{1,2,3}



“Urine tests are no longer necessary as part of the screening algorithm for identifying monoclonal gammopathies”

- Katzmann *et al*, *Mayo Clin Proc* 2006.⁵

Sensitivity of free light chain measurements in the detection of monoclonal gammopathies using normal ranges*			
Diagnosis	Study	N	Abnormal Free Light Chain Ratio, %
Intact Ig MM	Mead <i>et al</i> ⁶	493	96**
Light chain MM	Bradwell <i>et al</i> ⁷	224	100
Light chain myeloma	Tate <i>et al</i> ⁸	23	100
Light chain myeloma	Abraham <i>et al</i> ⁹	28	100
Nonsecretory MM	Katzmann <i>et al</i> ¹⁰	5	100
Nonsecretory MM	Drayson <i>et al</i> ¹¹	28	68
AL amyloidosis	Katzmann <i>et al</i> ¹⁰	110	91
AL amyloidosis	Lachmann <i>et al</i> ¹²	262	98
AL amyloidosis	Abraham <i>et al</i> ¹³	95	91
Light chain deposition disease	Katzmann <i>et al</i> ¹⁰	7	100
Light chain deposition disease	Katzmann <i>et al</i> ¹⁴	19	89
Smoldering MM	Katzmann <i>et al</i> ¹⁰	72	88
Plasmacytoma	Dingli <i>et al</i> ¹⁵	116	47
MGUS♦	Rajkumar <i>et al</i> ¹⁶	1148	33

A summary of numerous studies using **Freelite**.

This research was originally published in *Clinical Lymphoma & Myeloma*: Jagannath S. Value of Serum Free Light Chain Testing for the Diagnosis and Monitoring of Monoclonal Gammopathies in Hematology.

Clinical Lymphoma and Myeloma 2007; **8**:518-523

* Katzmann *et al*¹⁴

** Abnormal concentration and / or ratio

N = number of patients

Ig = Immunoglobulin

MGUS = Monoclonal Gammopathies of Undetermined Significance

♦The **Freelite** assay is not FDA cleared for use in risk stratification of MGUS patients in the USA.

Manage your patients accurately and easily

Freelite can be utilised as a rapid indicator of response to treatment in the majority of Multiple Myeloma patients. Free light chains have a half life of just 2-6 hours and have been shown to reflect tumour killing more rapidly than quantification of intact immunoglobulin.⁶

- **Freelite** can be used to assess response to treatment in the majority of Multiple Myeloma patients⁶
- **Freelite** can be used to identify and monitor a high proportion of Nonsecretory Myeloma patients¹¹
- **Freelite** can be used to monitor Light Chain Multiple Myeloma patients easily using a simple serum sample⁷
- **Freelite** can enable the assessment of treatment options earlier for patients who are failing to respond¹⁷
- **Freelite** can identify relapse earlier^{6,8,18}
- **Freelite** can identify patients who, upon relapse, switch to production of FLCs only (light chain escape)^{19,20}

Benefits of measuring free light chains to monitor response to treatment	
Benefit	Detail
Incorporated into Response Criteria Guidelines	Baseline studies needed for all patients for later assessment of stringent CR; more frequent sampling for patients who were unmeasurable using other methods
Rapid Indication of Response	Involved free light chain concentration decreases weeks before intact Ig levels decrease
Sensitive Assessment of Residual Disease	Abnormal free light chain levels can persist despite negative immunofixation
Dose Reduction	Assess adequacy of response after dose reduction or (early) discontinuation of treatment
Early Marker of Relapse	Detection of relapse is possible months before immunofixation converts to positive
Identification of Free Light Chain Escape	A shift in secretion from intact Ig to free light chains can occur with relapse; periodic monitoring with serum free light chain testing can detect free light chain escape
Prognostic Indicator	Free light chain reduction by $\geq 50\%$ or normalization of the involved free light chain concentration after treatment signals better prognosis in AL amyloidosis

This research was originally published in Clinical Lymphoma & Myeloma: Jagannath S. Value of Serum Free Light Chain Testing for the Diagnosis and Monitoring of Monoclonal Gammopathies in Hematology.

Clinical Lymphoma and Myeloma 2007; 8:518-523

CR = Complete Response
Ig = Immunoglobulin

Identify your high risk patients quickly

Freelite can help identify patients with a high risk of progression and poor prognosis. Several recent studies have indicated its use as an independent marker of prognosis in Multiple Myeloma patients.

Author	N	Detail
van Rhee <i>et al</i> ²¹	301	"High baseline SFLC levels were a reflection of higher tumor burden, higher degree of disease aggressiveness and light-chain-only MM with its greater propensity for renal failure."
Kyrtonis <i>et al</i> ²²	94	"The 5-year disease-specific survival was 82% and 30% in patients with [serum free light chain ratio] sFLCR lower than and equal or greater than the median, respectively (P=0.0001). sFLCR was an independent prognostic factor."
Snozek <i>et al</i> ²³	790	"These findings suggest that the serum FLC ratio at initial diagnosis is an important predictor of prognosis in myeloma, and can be incorporated into the ISS for improved risk stratification."
Kyrtonis <i>et al</i> ²⁴	214	"In conclusion, baseline sFLCR appears to be an easily determined powerful, independent and very promising novel prognostic factor for survival in patients with newly diagnosed MM."
Dispenzieri <i>et al</i> ²⁵	273	"An abnormal ratio proved to be an independent predictor of adverse outcome - in the case of SMM - progression to active MM."

"Unlike baseline and follow-up analyses of serum and urine M-proteins, high sFLC levels at baseline-reflecting more aggressive disease- and steeper reductions after therapy identified patients with inferior survival"

- van Rhee *et al*, *Blood* 2007.²¹

Risk stratify your MGUS patients with Freelite[♦]

An abnormal serum free light chain ratio has been identified as an important, independent risk factor for progression of MGUS to myeloma or related malignancies.¹⁶

Risk group	N	Absolute risk of progression at 20 years*
Low (serum M protein <15 g/L, IgG subtype, Normal FLC ratio)	449	2%
Low intermediate risk (Any 1 factor abnormal)	420	10%
High intermediate risk (Any 2 factors abnormal)	226	18%
High risk (All 3 factors abnormal)	53	27%

This research was originally published in *Blood*: Rajkumar *et al*. Serum free light chain ratio is an independent risk factor for progression in monoclonal gammopathy of undetermined significance. *Blood* 2005; **106**:812-817
©2005 The American Society of Hematology.

N = Number of patients
*accounting for death as a competing risk

♦The **Freelite** assay is not FDA cleared for use in risk stratification of MGUS patients in the USA.

Compliance with International guidelines

The International and UK guidelines for AL amyloidosis recommend that all patients should have a serum free light chain measurement as part of their initial laboratory investigation and to assess response to treatment.^{26,27}

The British Journal of Haematology guidelines on the diagnosis and management of Multiple Myeloma (2005) state that serum free immunoglobulin light chain measurement can be used as an alternative to quantifying urinary light chains.⁴

The National Academy of Clinical Biochemistry guidelines propose the use of free light chains in the diagnosis and follow-up of Nonsecretory Myeloma, MGUS♦ and amyloidosis.²⁸

In 2006, the response criteria for the assessment of clinical outcomes in Myeloma clinical trials were redefined.²⁹ Normalisation of the serum free light chain ratio is now included as part of the criteria for a stringent complete response (sCR) for all Myeloma patients.

Summary:

- Don't miss B cell dyscrasia. Use **Freelite** with SPE/CZE as part of your initial investigation.
- Eliminate the need for 24 hour urine samples when screening
- Identify high risk patients
- Identify efficacy of treatment sooner
- Identify relapsing patients early
- Compliance with International guidelines



♦The **Freelite** assay is not FDA cleared for use in risk stratification of MGUS patients in the USA.

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Assays are in use worldwide in reference laboratories,
many myeloma centres and hospital laboratories.
Visit our website to find your local supplier:

www.freelite.co.uk

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