

M-proteïne nabespreking

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Periode 2009.4 t/m 2012.3:

- 4 rondzendingen per jaar, 72 deelnemers
- Elke rondzending 3 monsters, soms met casus (A,B,C)
- Per rondzending 2 monsters bereid door UMCN 1 monster door UMCU
- Invoer via Qbase
- NIEUW: rapportage via Qbase sinds 2010
- NIEUW: Vrije Lichte Keten Kappa en Lambda bepalingen sinds 2010

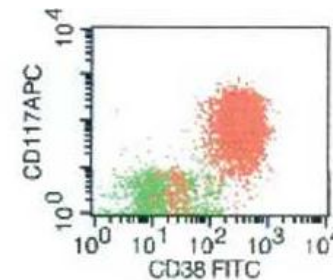
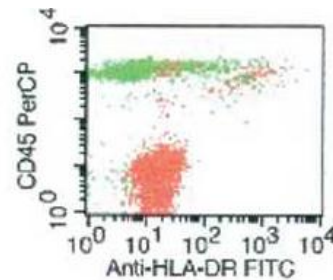
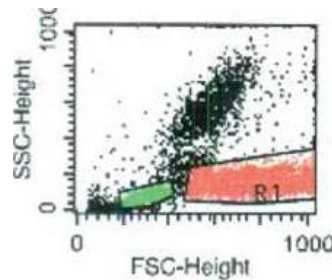
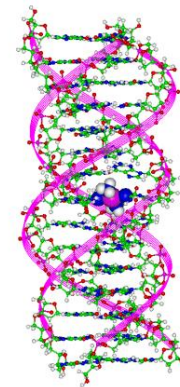
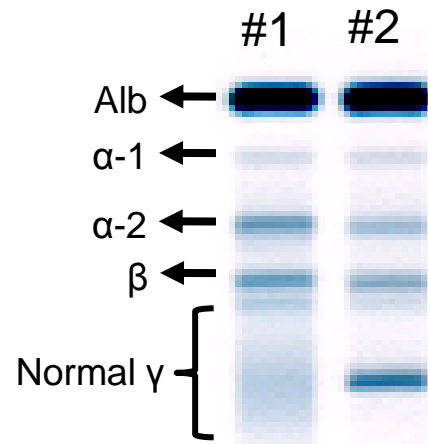
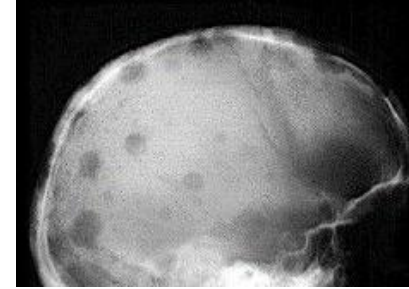
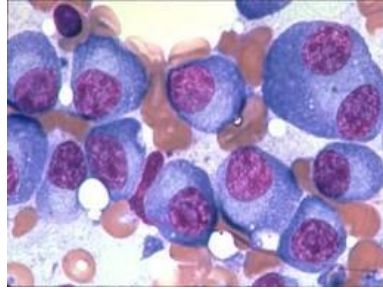
Inventarisatie:

- Typering M proteïne
- Kwantificering M proteïne
- Kwantificering Vrije Lichte Ketens (VLK)
- Soms additionele vraag

Wat is er rondgestuurd:

- IgG-K 6x
- IgG-L 7x
- IgM-K 4x
- IgM-L 1x
- IgA-K 4x
- IgA-L 1x
- Geen MPR 9x ***
- VLK-L 2x
- VLK-K 1x
- Oligoclonaal 1x

Diagnostiseren van een Multipel Myeloom



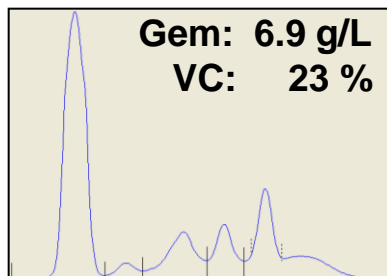
Monoklonale gammopathie: follow-up en therapie-respons

Durie, Leukemia 2006, 20, 1467-1473

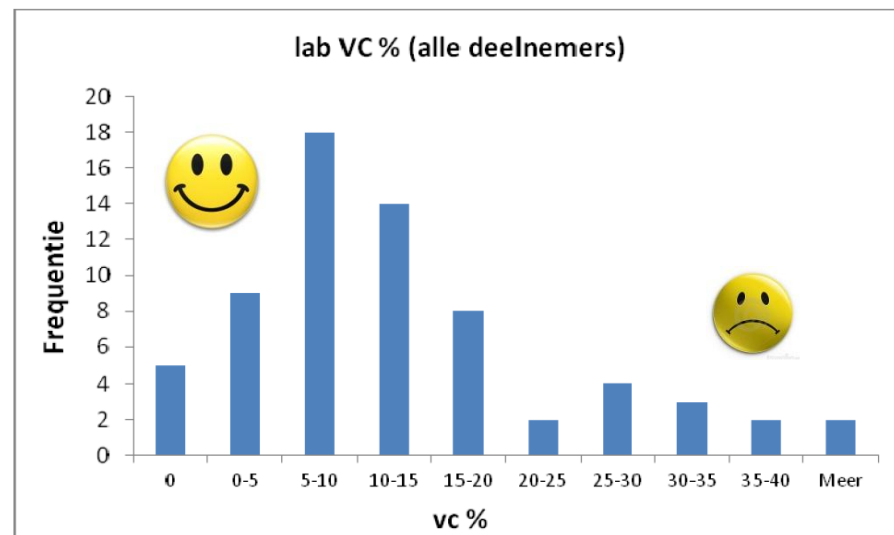
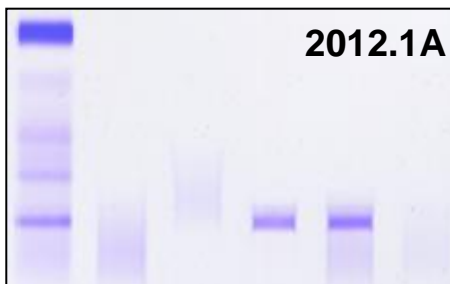
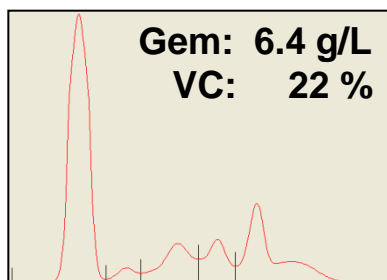
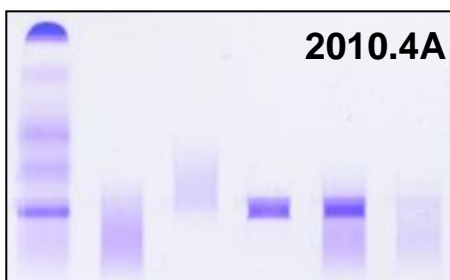
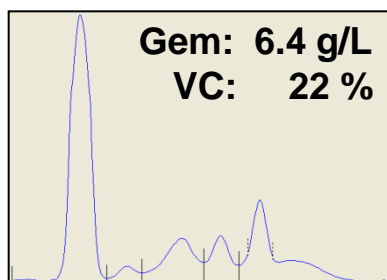
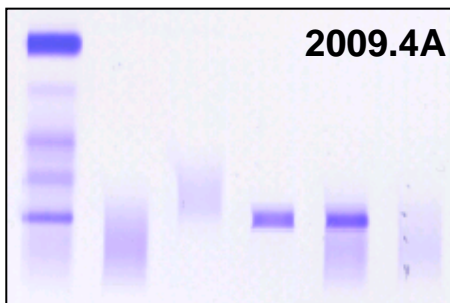
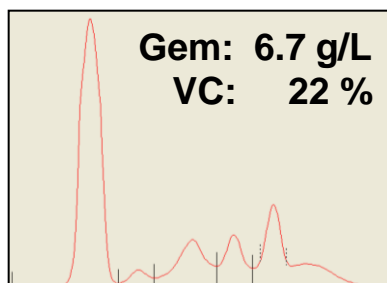
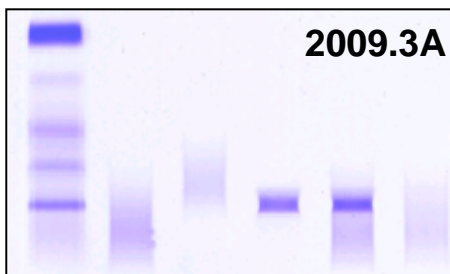
Table 5 International Myeloma Working Group uniform response criteria: CR and other response categories

<i>Response subcategory</i>	<i>Response criteria^a</i>
sCR	CR as defined below plus Normal FLC ratio and Absence of clonal cells in bone marrow ^b by immunohistochemistry or immunofluorescence ^c
CR	Negative immunofixation on the serum and urine and Disappearance of any soft tissue plasmacytomas and $\leq 5\%$ plasma cells in bone marrow ^b
VGPR	Serum and urine M-protein detectable by immunofixation but not on electrophoresis or 90% or greater reduction in serum M-protein plus urine M-protein level <100 mg per 24 h
PR	$\geq 50\%$ reduction of serum M-protein and reduction in 24-h urinary M-protein by $\geq 90\%$ or to <200 mg per 24 h If the serum and urine M-protein are unmeasurable, ^d a $\geq 50\%$ decrease in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria If serum and urine M-protein are unmeasurable, and serum free light assay is also unmeasurable, $\geq 50\%$ reduction in plasma cells is required in place of M-protein, provided baseline bone marrow plasma cell percentage was $\geq 30\%$ In addition to the above listed criteria, if present at baseline, a $\geq 50\%$ reduction in the size of soft tissue plasmacytomas is also required
SD (not recommended for use as an indicator of response; stability of disease is best described by providing the time to progression estimates)	Not meeting criteria for CR, VGPR, PR or progressive disease

Reproduceerbaarheid



ELP G A M K L

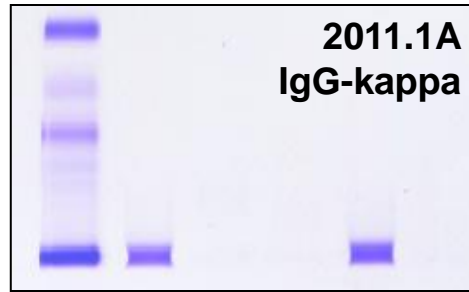
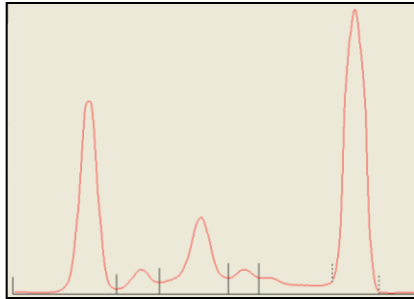


Gemiddelde VC binnen 1 lab over 4 metingen: 14 %

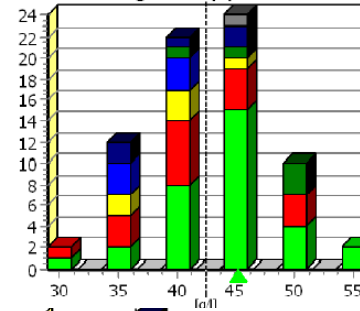
**Nieuwsgierig naar eigen lab VC?
Zie rondzending 2012.1A**

VC's: de ene IgG-kappa is de andere niet...

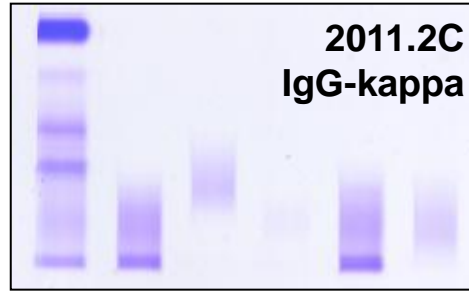
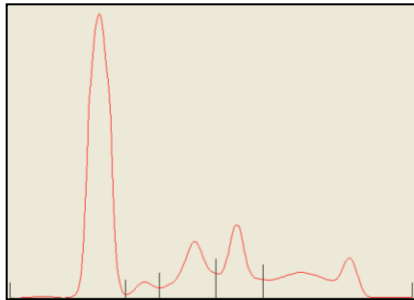
ELP G A M K L



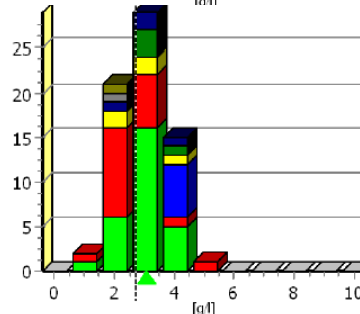
2011.1A
IgG-kappa



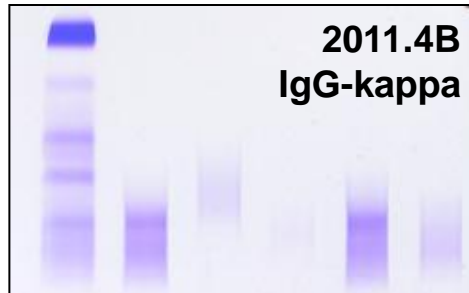
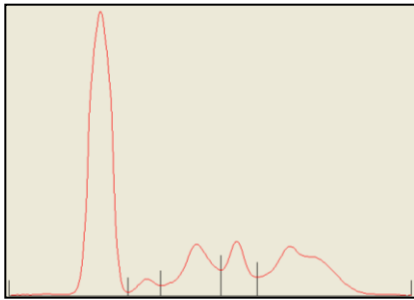
>95% IgG-kappa
Gem: 42.4 g/L
VC: 13 %



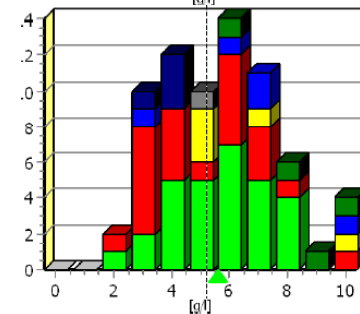
2011.2C
IgG-kappa



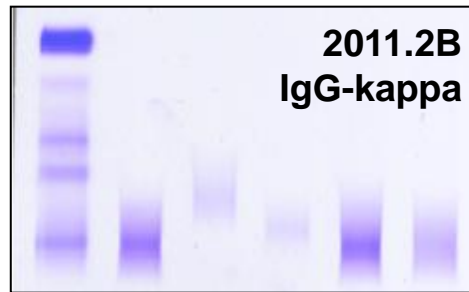
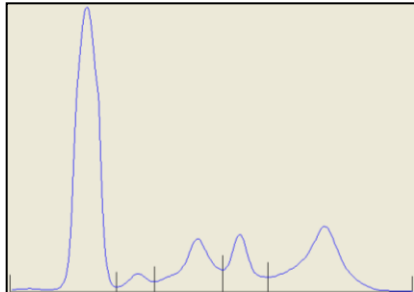
>95% IgG-kappa
Gem: 2.7 g/L
VC: 29 %



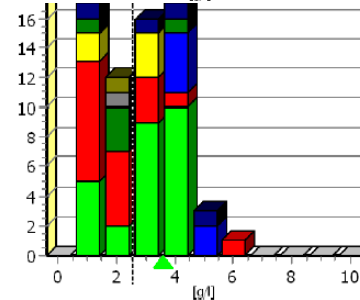
2011.4B
IgG-kappa



92% IgG-kappa
Gem: 5.5 g/L
VC: 40 %

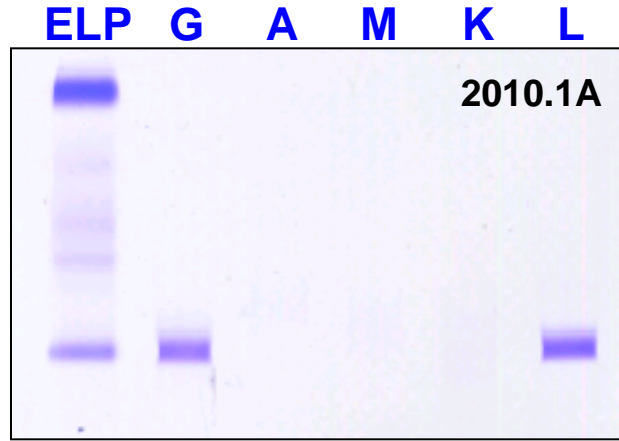
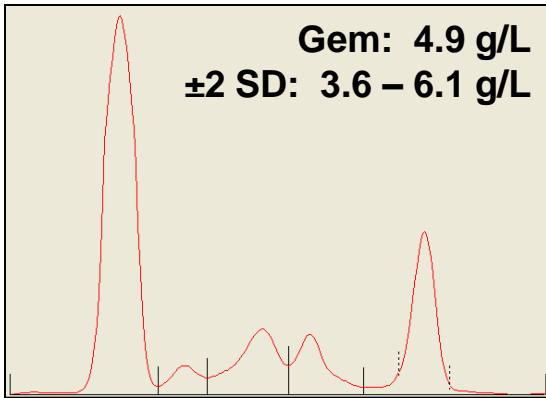


2011.2B
IgG-kappa

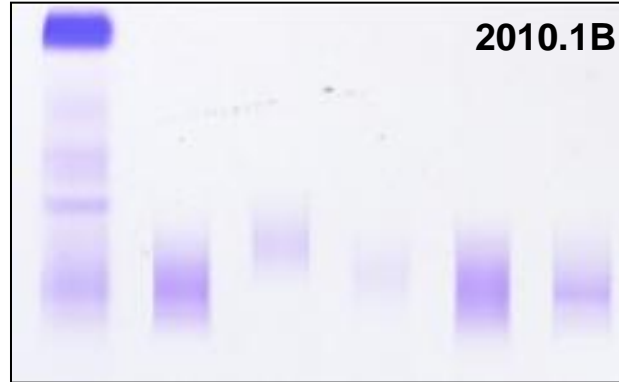
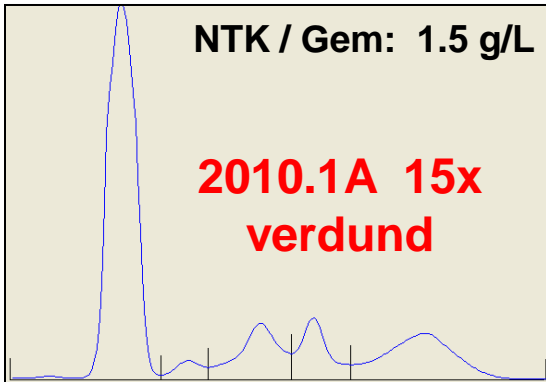
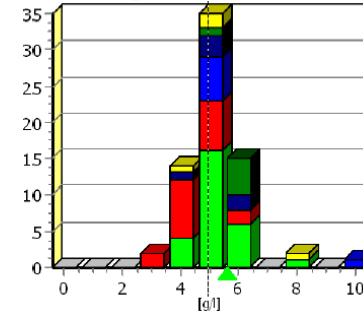


>95% IgG-kappa
Gem: 2.5 g/L
VC: 51 %

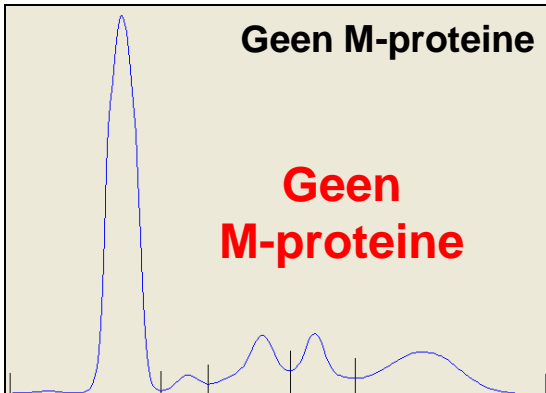
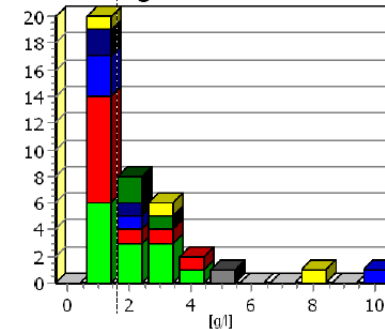
Kwantificeren na behandeling (oorspr. M-proteïne 30 g/L)



>95 % typeert correct IgG-lambda



87 % typeert correct IgG-lambda

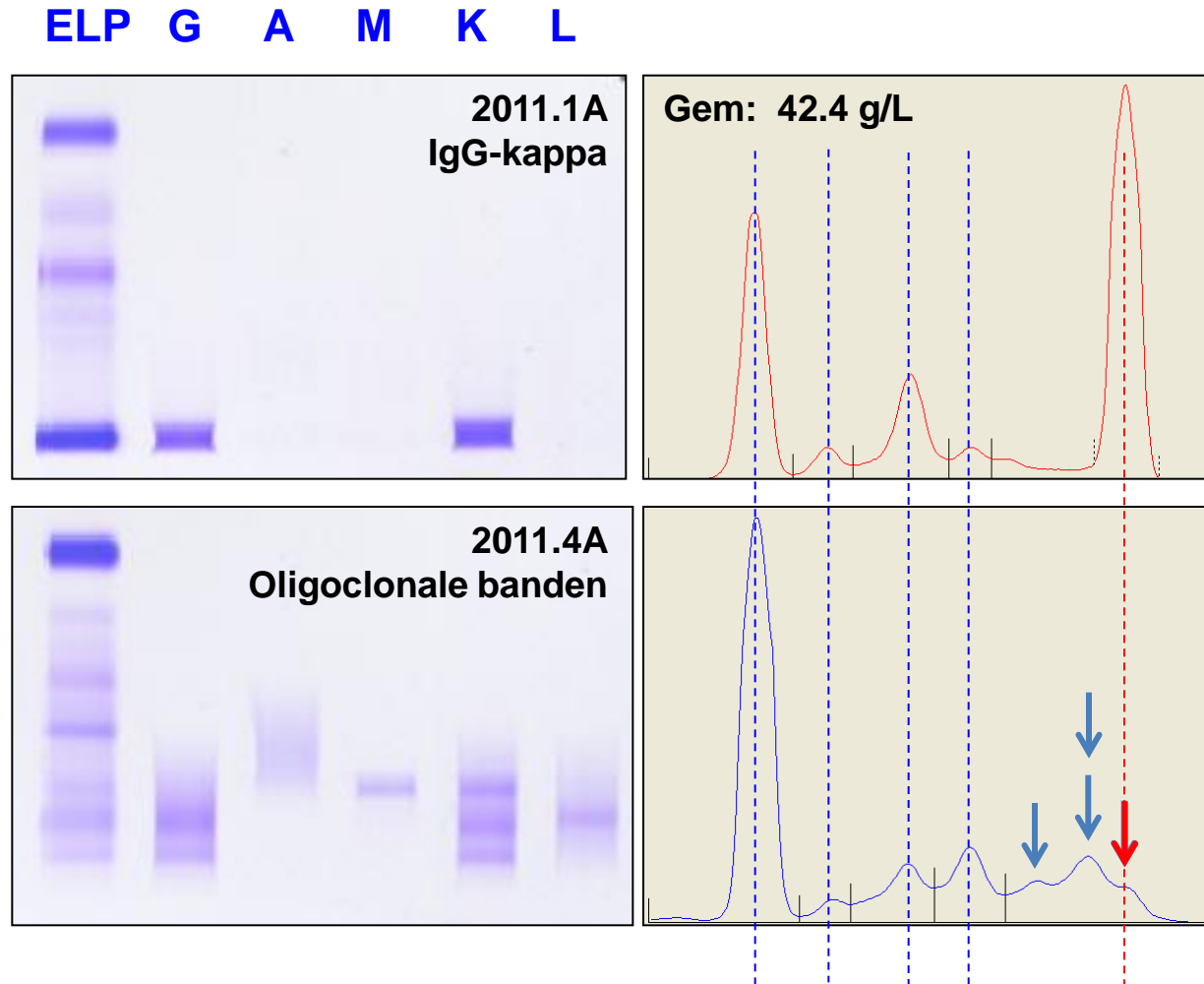


3 deelnemers typeren in-correct
een IgG-lambda

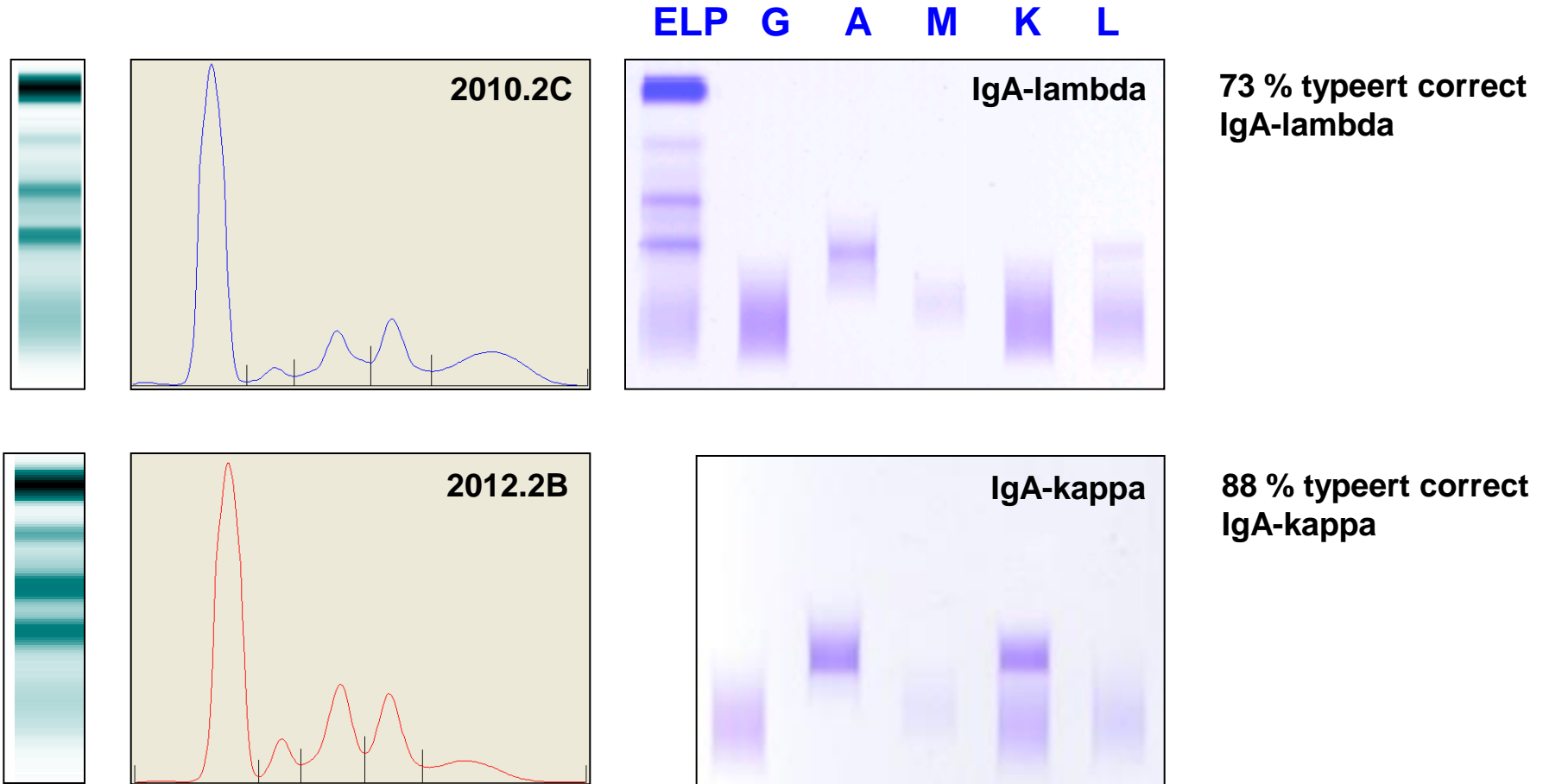


- > **95 % van de deelnemers rapporteert terecht geen M-proteïne**
 - Indien er een M-proteïne wordt gerapporteerd dan (doorgaans) 'NTK'

Vervolgen van een bekend M-proteïne



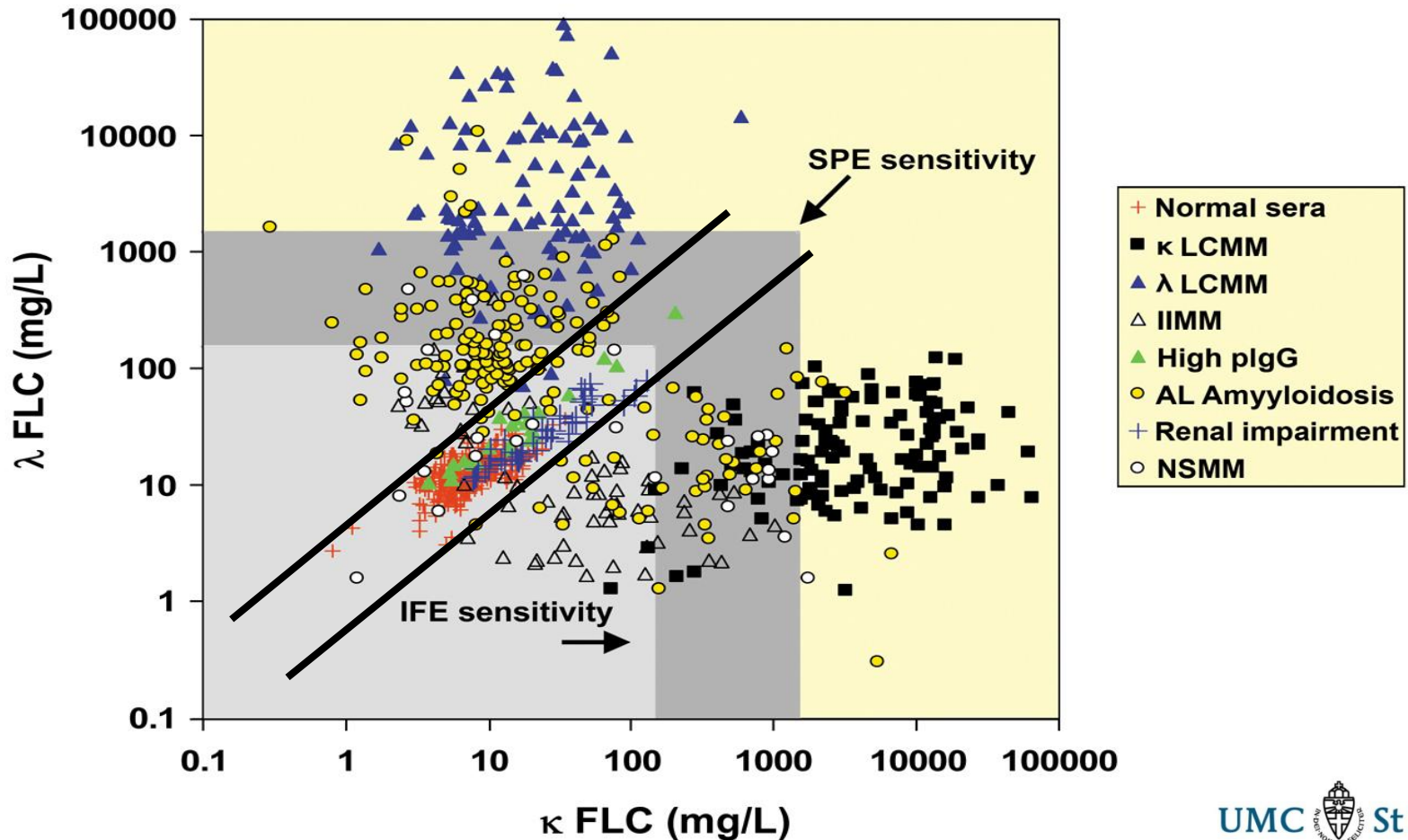
- Aan of afwezigheid van oorspronkelijke M-proteïne bepaald beleid
- Goed archief is belangrijk voor vervolgen van een bekend M-proteïne



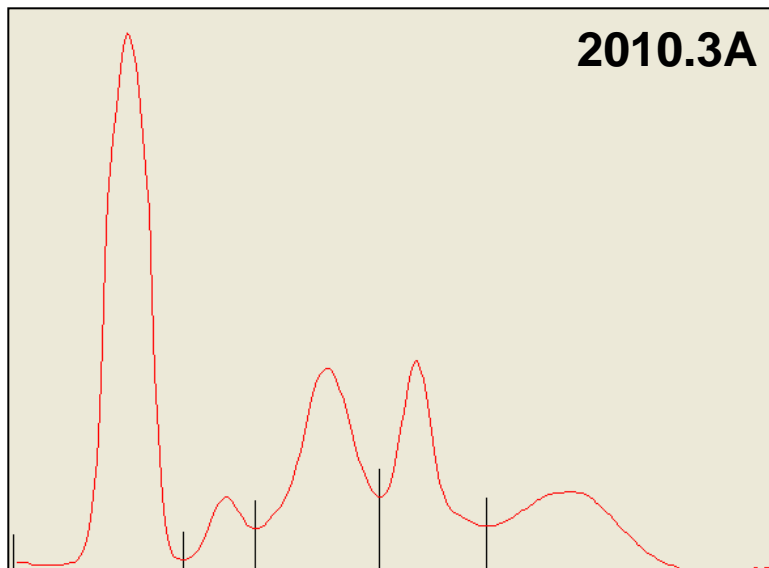
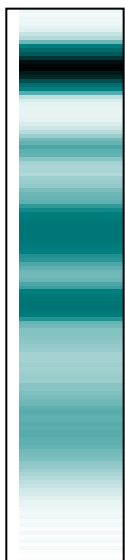
- M-proteine wordt gemist indien ESP niet kritisch bekeken
- Kwantificeren is lastig, spiken is niet mogelijk...
- 'Second best' is immunochemisch totaal IgA (cave polyclonaal IgA)

Sinds 2010 tevens sVLK bepalingen in MPR rondzending

Method	Kappa	Lambda	Diagnostic requirement
SPE	500-2,000mg/L	500-2,000mg/L	monoclonal band
IFE	150-500mg/L	150-500mg/L	monoclonal band
FLCs Nephel.	1.5mg/L	3.0mg/L	abnormal κ/λ ratio



Geen M-proteïne?

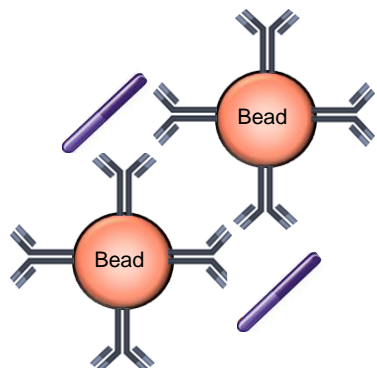


'penta'



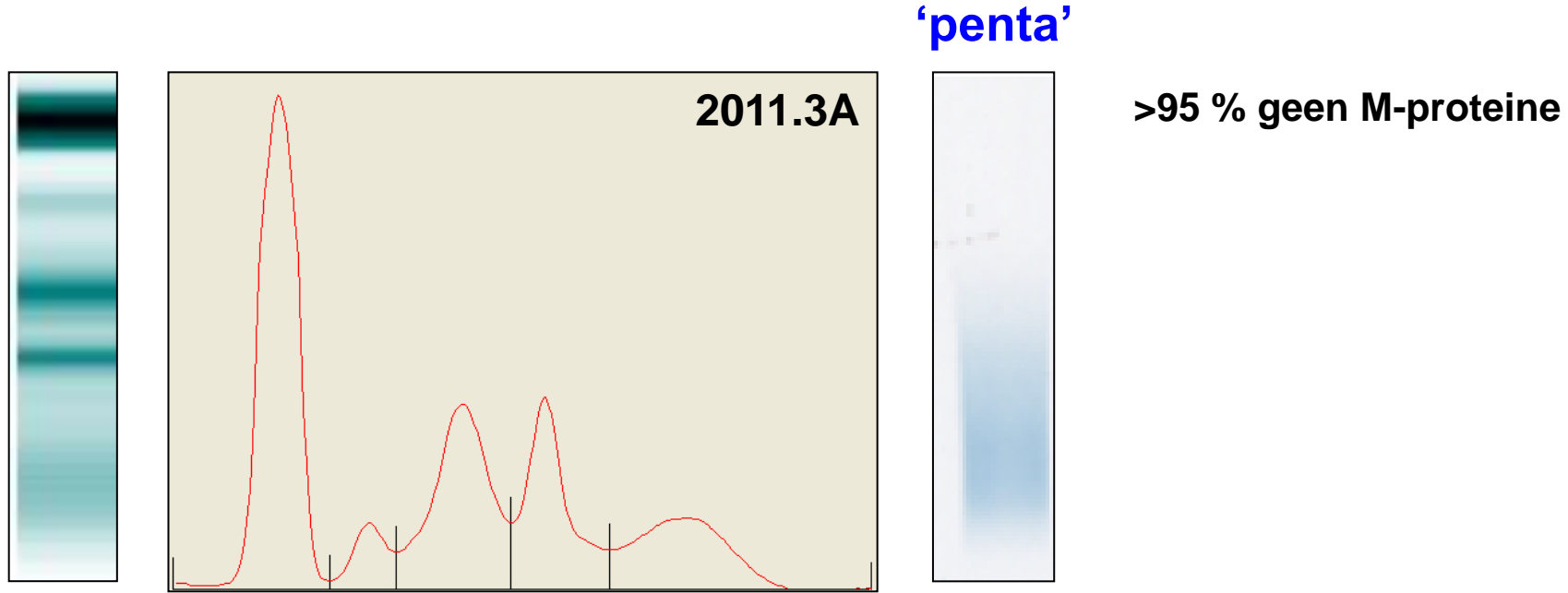
of IF zeker geïndiceerd want casus-beschrijving zeer suspect...!

sVLK nefelometrie

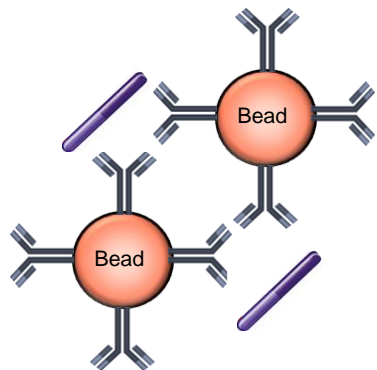


	<i>REF values (freelite)</i>	2010.3A
Free kappa:	3,3 – 19,4 mg/l	295 mg/l (VC 14%)
Free lambda:	5,7 – 26,3 mg/l	9 mg/l
Ratio:	0,26 – 1,65	34

Polyclonaal VLK Kappa + Lambda

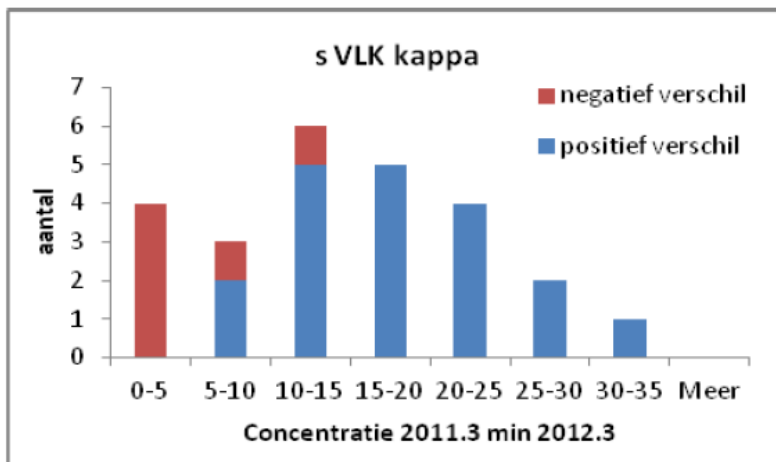


sVLK nefelometrie



	REF values (freelite)	2011.3A	
Free kappa:	3,3 – 19,4 mg/l	79,3 mg/l	} Normale ratio: niet suggestief voor VLK M-proteine
Free lambda:	5,7 – 26,3 mg/l	77,8 mg/l	
Ratio:	0,26 – 1,65 0.37 – 3.1 (nierfalen)	1,0	

Bepaling	2011.3 A		2012.3 A	
	Gemiddelde	V.C. (%)	Gemiddelde	V.C. (%)
IgG (g/L)	9,41	5,9	9,34	7,2
IgA (g/L)	1,81	4,5	1,80	4,5
IgM (g/L)	0,73	7,9	0,71	6,7
Totaal eiwit (g/L)	63,8	3,2	63,9	3,3
Albumine spectrum (g/L)	39,6	6,1	39,3	7,1
α 1-globuline (g/L)	2,5	29,7	2,6	30,7
α 2-globuline (g/L)	7,5	7,3	7,7	9,2
β -globuline (g/L)	5,9	12,8	5,7	9,4
γ -globuline (g/L)	8,5	16,7	8,4	14,3
sVLK kappa (mg/L)	79,3	15,6	91,3	15,6
sVLK lambda (mg/L)	77,8	19,5	76,7	13,4
Ratio (kappa/lambda) (ratio)	1,003	12,6	1,135	12,9



Conclusie:

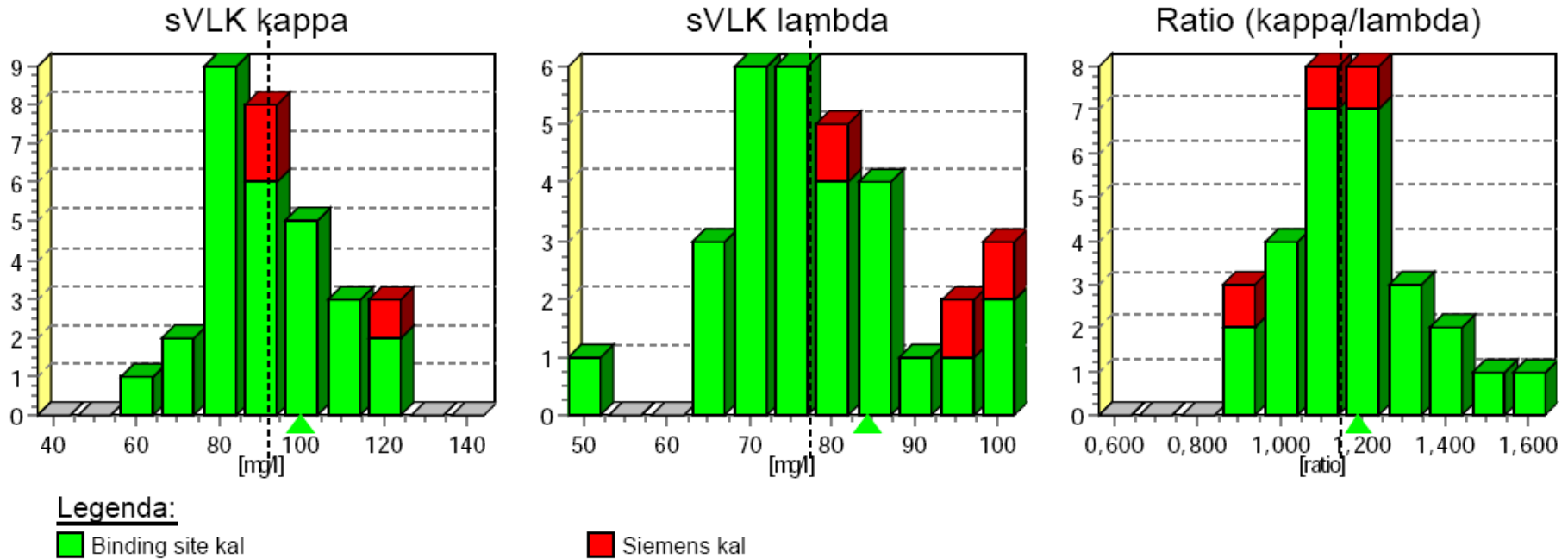
- Goede reproduceerbaarheid over alle parameters...
- Behalve sVLK kappa
- Niet veroorzaakt door enkele uitschieters

- Verklaring?

- Tate et al. Clin Biochem Rev 2009

Sinds 2012 naast Freelite (TBS) tevens N latex (Siemens)

2012.3A

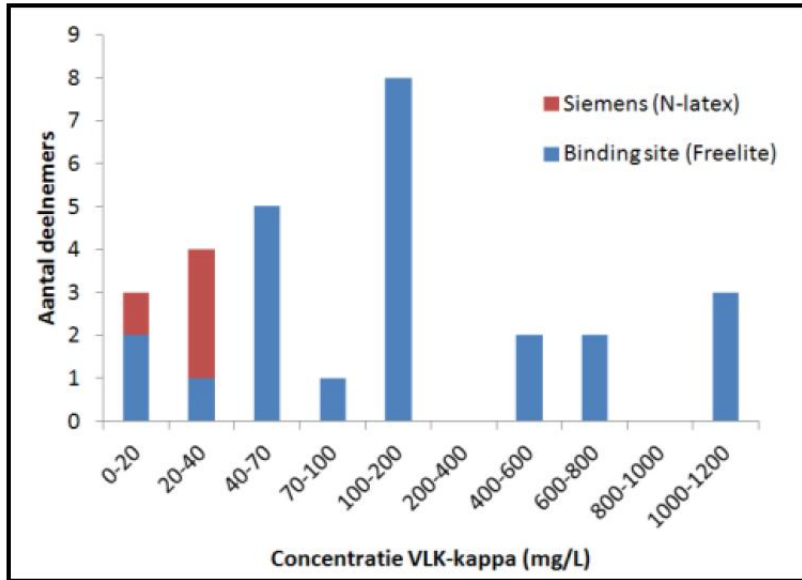
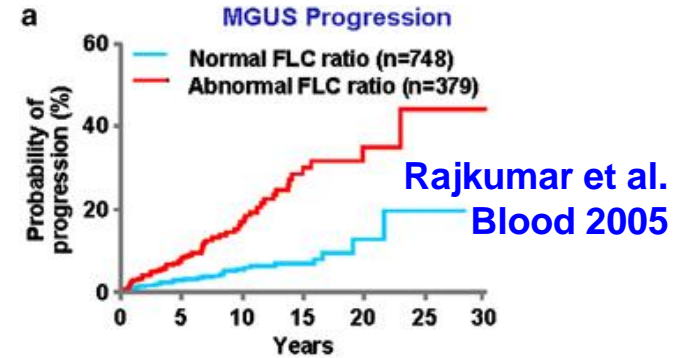
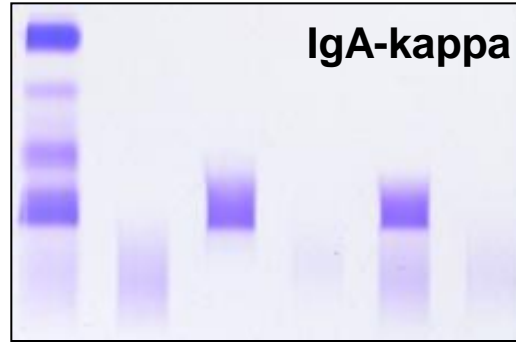
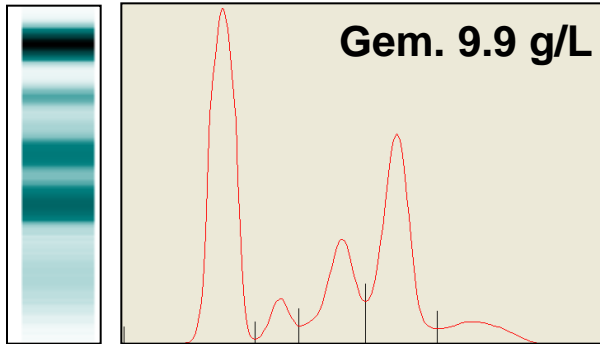


- Het is bekend dat er verschillen zijn in kwantificering tussen TBS en Siemens
- Dit zal tot uiting komen als een patiënt wisselt van ziekenhuis
- ...en bij de rondzendingen...

sVLK metingen in aanwezigheid van een intact Ig



2012.2A



Verdunning	The Binding Site (Freelite) Gemeten op BNII	Siemens (N-latex) Gemeten op BN ProSpec
1:100 (= initiele verdunning)	80 mg/l	21 mg/l
1:200	163 mg/l	n.t.
1:300	n.t.	62 mg/l*
1:400	264 mg/l	n.t.
1:800	308 mg/l	n.t.
1:2000	456 mg/l	n.t.
1:4000	472 mg/l	n.t.

Conclusie:

- Sterke non-lineariteit van sVLK bepalingen is mogelijk in aanwezigheid van intact M-proteïne
- Interferentie is concentratie afhankelijk, vanaf ca 10 g/L intact M-proteïne kunnen problemen ontstaan
- Mate interferentie is isotype afhankelijk IgA>IgM>IgG
- sVLK-kappa assay is gevoeliger voor dit fenomeen
- Bij zowel Freelite als N latex assay
- Fenomeen alleen zichtbaar indien je meet in meerdere verdunningen...

Vercammen et al. Clin Chim Acta 2011
Jacobs et al. Clin Chim Acta 2012

Met dank aan:

**Corrie de Kat Angelino
Gertrude van der Wiel
Ina Klasen
Renate van der Molen**

Ondersteuning SKML

Tevens een interessant sample geschikt voor de M-proteïne rondzending?

Zeer welkom!

- **100 ml serum nodig per monster (!)**
- **Echter, samples kunnen ook gespiked worden in normaal serum. In dat geval minder serum nodig.**
- **Graag contact:**

H.Jacobs@labgk.umcn.nl

Scoresysteem

Rapportage	Score
M-proteïne correct getypeerd	2
Extra M-proteïne met hetzelfde type	0
Alleen zware keten genoemd	1
M-proteïne gemist	-1
M-proteïne fout getypeerd	-1
Ten onrechte 2 ^e M-proteïne gemeld	-1
Kwantificering (van correcte M-proteïne)	1